THE BRITISH JOURNAL

OF

OPHTHALMOLOGY

JULY, 1934

COMMUNICATIONS

CERTAIN CLINICAL FEATURES OF THE NORMAL LIMBUS

BY

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Continued from p. 341

The Vascular Plexus of the Limbus

A few points concerning the limbus-plexus of Fig. 16 may now be considered. Mention may be made of the large centrifugal vessel M; it lies stereoscopically mid-way between the surface of the conjunctiva and the surface of the sclera. Some of the deeper basal vessels of the limbus-plexus, and also some of the episcleral vessels into which they lead, are drawn in hatched lines. The tributaries N and O to the vessel M are worth noting; they are an example of a feature commonly seen.* Two vessels run side by side as one, having a common binding "coat." When the blood is not circulating in them, or when it is absent temporarily in one, the double nature of the channel is apparent. It is not uncommon to find fused conjunctival vessels which for a part—sometimes a very long one—of their course are treble or quadruple in bore, the whole appearing as one large expanded vessel when the circulation is abundant. A similar principle may be seen in the case of the ring s′ – sd – d′ which measures 0·1 mm. across its longest diameter. The two channels, s and d—s being

*An error of omission occurred in printing this part of the block; a note of correction will appear in the August issue.

the superficial and d slightly deeper—together form the segment sd, and for this short distance (sd) they run in a common union, the blood here going in opposite relative directions in the two; and they reunite to leave the opposite side of the ring in similar close association along sd', the blood here going in the same relative direction in each. It is quite easy to appreciate this relationship stereoscopically, the one component here lying precisely over the other. In other similar instances of concomitant association of vessels of the limbus-plexus, they may be side by side in the same plane instead of being superimposed one on the other.

The case of Fig. 16 affords a good example of a not uncommon type of limbus-plexus, *i.e.*, one in which a single relatively large vessel along the corneal border of the plexus conveys blood in one direction concentric with the limbus. Such a vessel in the course of embryonic development is probably in part formed by successive linking of the transilient summits of conterminous loops; it is at first insignificant and sinuous, but with establishment of the dominant continuity of its individualized circulation its successive angular salients tend to become more and more obtuse in aiming at a direct alignment. (The details in Fig. 16 were correctly depicted in nearly all their proportions and angular relations). Under normal conditions only this concentric marginal vessel conveys blood, and the channels of the net lying on the conjunctival side of it are usually empty; but they fill up readily under any circumstances increasing the superficial vascularity of the eye.

This condition is imitated by certain types of pathological superficial corneal invasion from the limbus above, the final state settling down with a major transverse corneal vessel running concentrically with the limbus and being formed by a serial anastomosis between the distal apical constituents of the feeding loops whose basal or proximal portions eventually play a minor rôle.

On the corneal side of this main marginal channel, in the normal example here drawn, some very fine loops are seen at U V W X Y and Z. They were nearly always empty in this particular person, but under rare circumstances they conveyed blood, especially the loops at Z and U. The very fine deep anterior ciliary afferent vessels ("a" 1, 2, 3 and 4) to these loops are evident. At the summit of Z is a very minute and all but invisible blind extension. This was at no time seen to convey blood. By analogy with pathological invasions, it represents a characteristic stage in the development of an immigrating vascular tube where it has just stopped short of full functioning encroachment. A similar feature is seen at W.

Another normal type of the limbus-plexus is seen in Fig. 20. Here the principle on which the final end-loops are built is noticeable. It will readily be seen how the blood, brought by the two

fine deep afferent vessels, a and a1, can readily discharge itself into the penultimate plexus-system without of necessity having to flow through the most remote (corneal) terminal loops. Fig. 21 shows other examples of normal terminal (corneal) capillary loops in the same subject.

(Figs. 20 and 21 were recorded in 1924 from a man, aged 45 years; I re-examined him in 1933 and although the tracks of the terminal end-loops were still discoverable, the blood had ceased to flow in many of them. It is my impression that a clinical opinion on the tendency to general arterio-sclerosis of any individual cannot be gained by an isolated inspection of the conjunctival and limbal capillaries; but some accurate information may perhaps be deduced concerning any one individual if minute records of the vessels, such as those here shown, can be made and remade from time to time as years go by—a procedure obviously too tedious for general adoption at present).

In some persons these loops have a dominatingly elongated character and are so uniformly spaced as to convey the appearance of a delicate marginal alphabetical frieze. As will be seen, the terminal loops display the general principle (applicable to normal and pathological systems) that as soon as the arterial capillary has turned back on its course, the diameter of the vessel at once increases. The flow of blood is so rapid in these small calibrated arterial vessels that it is seldom visible; but once the blood has entered the larger loops its relatively leisurely and purposeful flow is very easily seen. The blood having entered the plexus, the direction of its flow in any of the constituent parts is subject to whimsical variations according to local pressure-influences. It is by no means uncommon for the bulk even of these larger plexus-vessels to contain no circulating blood under average conditions. In one or more constituents of the network the blood may flow at one time in one direction, at another in the opposite: it may remain stationary or it may oscillate. These instances of hesitating, alternating, and reversing flow in many of the components of this normal network suggest the conclusion that the blood, once it is delivered by the invisibly rapid flow in the small calibrated arterial capillaries, pursues its leisurely flow in the plexus with adequate time to serve the metabolic purposes for which it has been brought rapidly to the particular region. On this account it might seem appropriate to name the coarser constituents of such a plexus, *i.e.*, all exclusive of the fine afferent arterial channels which are apt to be overlooked unless the observation is carefully made, the "metabolic vessels." The adoption of this nomenclature is further supported by the evidence of pathological corneal vascular invasions, whose principle is commonly much the same—save that they may at times reach out

to distances far in advance of their normal initial base—*viz.*, a dilatory system served with rapid delivery (sometimes mainly terminally or apically, sometimes in all its parts) by very fine arterial channels whence transition of calibre is relatively abrupt. It is, perhaps, reasonable to assume that the architecture of a pathological vascular invasion may be adapted in anticipation of the metabolic functions which it will be called upon to serve. If this conception is acceptable, there is reason for refraining from the use of the word "venous" in speaking of the larger components of a capillary system before they have materially converged to form main conducting channels of departure (such, *e.g.*, as the large vessel M, Fig. 16). If the trabecular loops serve a purpose—and are not some sort of vestigial remnants no longer useful—then the larger (usually centripetal) component of each might be included with the "metabolic system."

At first sight the functional and morphological appearance of this plexus at the limbus conveys an impression that it is "venous" in character, *i.e.*, excluding the fine arterial afferent channels which are inconspicuous, it consists of a net-work of relatively coarse capillaries leading, peripherally, direct into larger episcleral vessels whose blood is flowing mainly centrifugally away from the net. In further suggestion of the seemingly "venous" character of this plexus, it is joined here and there by the numerous apparently "venous" (*i.e.*, large calibred) efferent components of the various afferent-efferent conjunctival loops described, and the rate of blood flow is leisurely in these components when compared with the rate in the corresponding afferent arterial components. It is true that most of these conjunctival loops, save some of the isolated intratrabecular loops, receive minute accessory tributaries from the conjunctiva, but often in a manner suggestive of the access being contingent and incidental, rather than fundamental. I would like to suggest that the efferent components of these conjunctival loops, though perhaps phylogenetically belonging to the "venous" side of a capillary system, have become specialized in the conjunctiva to facilitate oxygenation of the blood as it passes through them on its way to the limbus-plexus. Moreover, considered in relation to a time-factor, the rate of blood flow is relatively slower if the course is elongated by a loop-formation even if no part of that course undergo any increase in diameter, *i.e.*, a given unit of blood will stay longer near the surface in proportion with the mere length of the surface-loop which it traverses. The epithelium of the conjunctiva is very thin —only three cells deep. I have hesitated to make this suggestion in print without seeking further opinions, *e.g.*, that of Dr. F. G. Chandler, on the question of the absorption of gases through the pleura. From what I can gather by analogy with other parts of

the body there is not, *prima facie,* any apparent objection to this suggestion in principle which I will not discuss at length, save to add that Sir Stewart Duke-Elder, whose opinion I have sought, sees no fundamental objection to it. He adds that it has been shown that the corneal epithelium has the property of actively absorbing oxygen and that there is no apparent reason why the thinner conjunctival epithelium should not do so. The colour of the blood in all the efferent components of afferent-efferent conjunctival loops tends to be red and not purple; and the lasting redness of a spontaneous subconjunctival haemorrhage, when it is not very gross and extensive, is a matter of common knowledge. I do not suggest that the conjunctival vascular architecture is ideally specialized to facilitate direct oxygenation of its blood to the fullest capacity that could be devised if this were the main aim in its design, but rather that, among the factors which have contributed to the evolutionary specialization of the design, a partial subservience to this particular function may have contributed its quota in moulding the phylogenetic material available. The fact that trabeculae are not found in all individuals, and that, when they are found, not all of them contain vascular loops (see, *e.g.,* Fig. 12) suggests that their vascular function is possibly vestigial; but the long conjunctival loop-system is practically a constant characteristic. It may be conjectured that the blinking movements of the lids, by compressing and decompressing both the vessels and the lax mobile areolar tissue in which they lie, influence the gaseous interchange in this primitive superficial "respiratory" function. It is worth considering the possibility of treating certain surgical and pathological conditions of the eye on the basis of these conjectures.

There is a recurrent acute affection of the conjunctiva—as far as I know not clinically recognized except that it gets labelled "conjunctivitis"—which is characterised by great dilatation of the "metabolic" constituents of the conjunctival vascular system in the absence of any surface discharge or other apparent surface trouble. When, in inflammation of the eye, these long, fairly straight metabolic conjunctival vessels dilate, they also tend to become flexuous suggesting that they perhaps undergo an intrinsic longitudinal expansion as well as transverse dilatation.

In making this rather lengthy approach to this subject I have succumbed to the temptation to present a selection of simple clinical observations somewhat in the order in which they chanced to unfold themselves when I made them with no particular pre-formed ideas in view. I would like to add one final example from records of a type which seemed to support this view after those already given had afforded inferential evidence leading up to its suggestion. In Fig. 22 an episcleral anterior ciliary artery A′ is seen dividing

into branches A, AA. (There were no trabeculae here in this subject.) The branch A loops forward and is quite superficial, *i.e.*, it is immediately under the conjunctival epithelium in its course A, B, C, CC. The portion ABC of this vessel, which is arterial in origin, increases to a diameter suggestive of a "metabolic" function. The movement of its blood could not be seen in this portion ABC, but from the origin of the vessel a southward flow could be inferred. Now the flow in the portion C - CC was southward and was usually very slow and "dilute"—*i.e.*, the corpuscles were not close packed—progressing usually in very short cardio-vascular periodic steps. The blood went rapidly southward in the portion C - CC only when the local vascular activity was more excitable than normal, *e.g.*, on one occasion when there was a small foreign body on the eye. Opposite B and C respectively two very tiny (only just visible) quite superficial vessels D and G branch off from this dilated "arterial" channel and if their course is followed it will be seen that they lead by way of vessels still superficial, *which receive no other tributaries,* to R and J, which empty into the limbus-plexus. The vessel GHJ undergoes an appreciable increase in diameter in its portion HJ. The flow of blood was rapid, and always in the direction shown, in the minute superficial connecting vessels G and D. Thus it can be inferred that the flow of arterial blood is relatively slow through the dilated portion ABC because of the mechanically restricted outlet, through the tiny vessels D and G, and of its functionally counterbalanced restriction through the southward outlet C - CC; the portion of this blood which passes on through G will again flow through another superficial channel of larger diameter H before it enters the limbus-plexus. Although peripheral connection is established with the purely conjunctival circulation at CC, it is quite clear that the arterial blood of the vessel A is mainly destined for the limbus-plexus and that its main purpose is seemingly not to give blood to, or receive it from, the conjunctiva through which it travels by a circuitous excursion. (Space need not be given to further description of this figure other than to add that AB is obviously of arterial origin; AD and VA form an afferent-efferent loop based on the limbus and not absolutely superficial in the conjunctiva until it is approaching the region of VC (but its fine arterial branch, AE, is very superficial) more peripheral to which, in the region of P, it spreads out into connections with the ordinary conjunctival circulation; it is evident how some of the arterial blood of AF can pass down to the region of VD which is directed towards the fornix. T is from a portion of the temporal marginal region of a limbus at about "3.15 o'clock"; AK and VG are an arterio-"venous" superficial conjunctival loop, AK becoming superficial in a curve from the episcleral artery Z; the

fine arterial branch LMN, from Z, will be noticed. The vessel W – X unites with VG at X whence in common union they plunge deep, perpendicular to the surface, to join the episcleral plexus vessel, OP. Fig. 23 is added as an additional example showing an *arterial* anterior ciliary episcleral connection at the limbus;

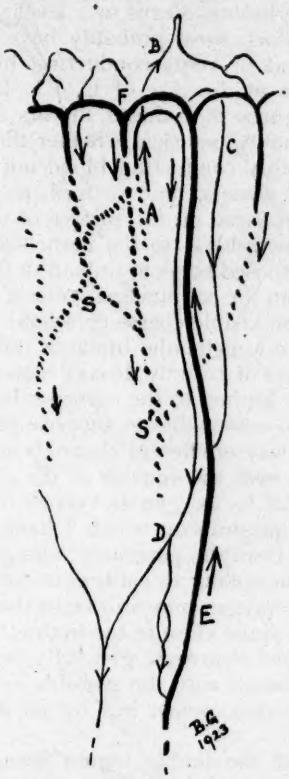

FIG. 23.

these are often not so easily seen as most of the other features described; A is the episcleral artery which curves forward to take a conjunctival course down to and beyond D; in part of its course it accompanies the conjunctival efferent vessel E; a branch, B, goes up to the marginal region of the plexus, and another branch, C, passes down to join the conjunctival efferent vessel E.

In concluding these remarks on the possible use made by local oxygenation of the blood I do not suggest that it be stressed too

much. The conjunctival loops are relatively not very numerous, and the suggestion is not one which is altogether compatible with the fact that the metabolic constituents of the conjunctival loops tend to join the basal or peripheral parts of the limbus-plexus rather than the final marginal or apical constituents; in fact, many of the larger conjunctival "veins," (*i.e.*, efferent constituents of long loops) join the limbus-plexus at a level where it merges with episcleral vessels which most probably have a function which is little more than that of veins conducting blood away from the plexus; this is seen in the case of E, E1, E2, E3, Figs. 2 and 3, and of other figures reproduced in this article. Even so, it might not unreasonably be asked whether these coarser episcleral vessels—which, visibly conducting blood not quite so red as that in the conjunctival vessels, tend to form an intercommunicating spread-out plexus of sorts, on the surface of the sclera over a considerable distance peripheral to the corneo-scleral junction—may possibly be thus disposed so as to unload in this plane the oxygen brought to them from the conjunctival vessels "round the corner;" in other words, these visible coarse episcleral vessels may possibly to some extent serve a metabolic function rather than merely that of efferent conductors of entirely deoxygenated blood from a metabolic region strictly limited to the corneo-scleral junction. In this connection it is also reasonable to suppose that the blood leaving the conjunctiva by way of efferent channels at the fornices to enter the episcleral veins near the equator of the globe, is probably not as yet so deprived of its oxygen as venous blood normally might be. This raises a question on which I have no knowledge, *viz.*, as to how far back from the periphery, along the homeward path, vessels gradually increasing in calibre are still capable of permitting transfusion of what oxygen may still be in them. It may be added, finally, that, except quite close to the limbus, the episcleral vessels have, for the sake of clearness, generally been omitted from the figures here reproduced, with the possible exception of Fig. 16 in which, in hatched lines, some, but by no means all, have been inserted.

As the vessels of the limbus-region furnish conjunctival and also sessile loops, it might be convenient to classify, as an "offshoot" from them, *i.e.*, one central to the region of the sessile loops, the finest, and often empty, corneal loops already referred to, terminating immediately beneath the marginal epithelium of the cornea. It would seem reasonable to regard these final corneal loops as not being essential for the nutrition of the cornea. It is expedient to look upon them as the final relics of the "leaders" of the advancing vascular invasion in the embryo which, having served their purpose, pass thereafter a dormant, and in the case of some, almost extinct rôle, ready to lead the way once more if

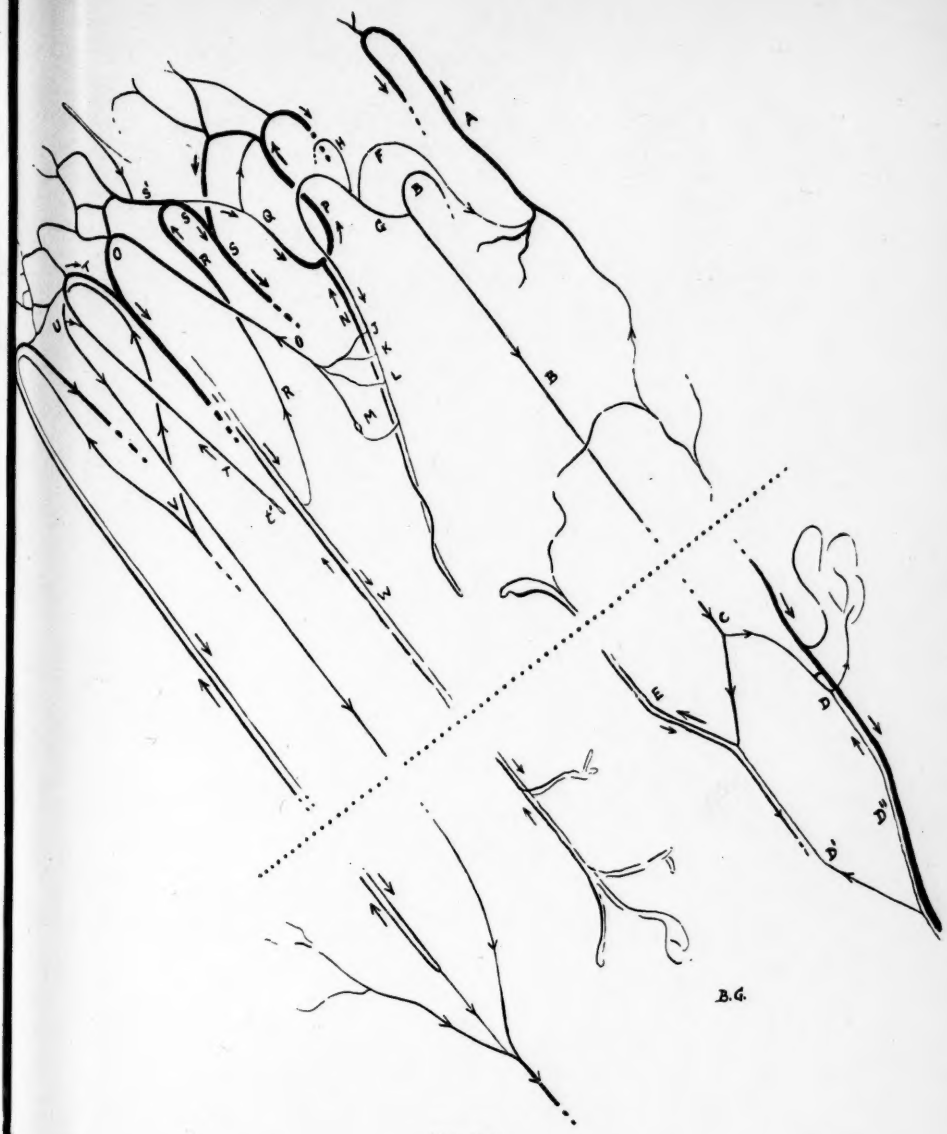

FIG. 18.

Mainly to show the destination of three anterior ciliary arterial vessels: B at its upper curved end leaves the episclera and arches forward to take a conjunctival course BC (giving off the branch G); the episcleral origin of W is not shown before it has come forward to run down superficially in the conjunctiva, this vessel being depicted here chiefly to show its recurrent branch R; V is shown in its episcleral position where it bifurcates into two branches which arch forward to take a downward course in the conjunctiva, one of them, at U, contributing the afferent component of the loop T—t'. A further feature shown in this figure is the transitional alteration of calibre of the vessels RR and Q.

This figure is described on pages 336 and 337.

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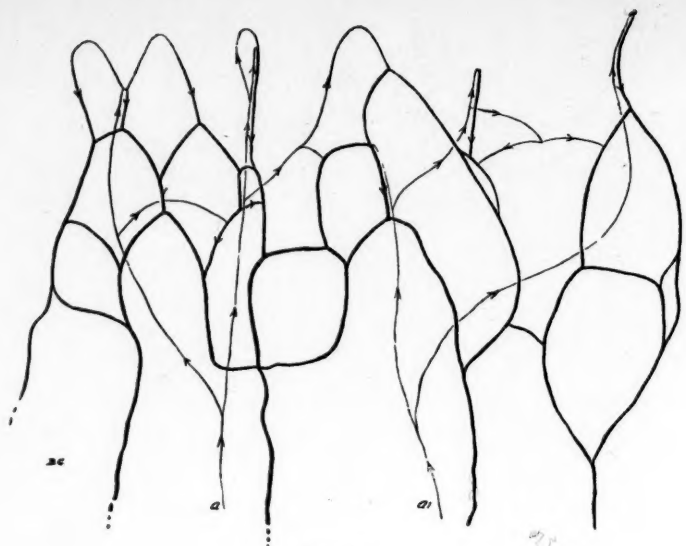

FIG. 20.

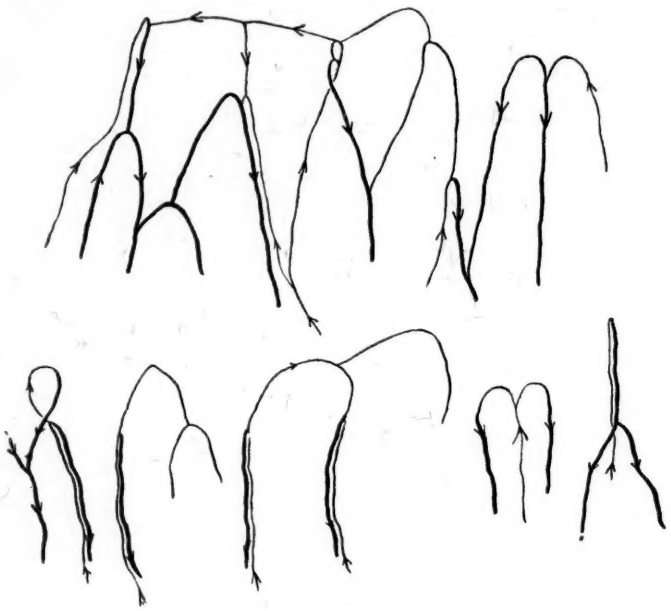

FIG. 21.

Terminal Marginal Corneal Loops.

Linear magnification: approximately ×135.

(The afferent channels in these two figures, particularly in Fig. 20, have not, in reproduction, come out as fine as they should be in relation to the thickness of the efferent ("metabolic") vessels. This is not due to lack of skill or care on the part of the publishers, but is unavoidable unless, *rather unnecessarily, a more costly method of reproduction be employed.*)

FIG. 22.

FIG. 29.

Peripheral refractile post-corneal rim in optical section

Linear magnification : approximately × **28.**

by chance later in life a pathological invasion in the homologous anatomical plane should claim their initiation in a further vascular advance. (This statement requires amplification and certain reservations for which there is not space here. It must be borne in mind that, under the elementary conditions of clinical observation, the proof that fluid is circulating in small vessels is afforded by no other means than seeing the blood corpuscles in movement. I have seen corpuscles held up at parts of developing capillaries by their impaction at sites transiently just too narrow to permit their passage. I think it not at all impossible that some of these finest end-loops—which under ordinary "quiet" circumstances may be too small in bore to transmit corpuscles—may sometimes have blood serum slowly percolating in them; indeed, this would be a reasonable supposition in keeping with the fact that such tiny vessels, both normal and pathological, may under circumstances of local vascular engorgement suddenly transmit visible corpuscular circulation after having failed to do so for a very long time—even after years in the case of some pathological capillaries. Vogt apparently refers to Koeppe having "no doubt in error" referred to a "blood-free lymph-vessel net at the limbus." It would be interesting to enquire if Koeppe—as a pioneer working at a time when terminological pitfalls were unpremeditated—might have had in mind this possibility concerning the terminal vessels when they are not dilated enough to transmit the largest solid elements to the blood.)

The Superficial Limbal Spur

The exact plane of the visible limbal network remains to be described. If the focused wide slit beam is cast on the limbus region, the superficial face of the block of light appears to be approximately as in Fig. 24. If the thin optical section is employed (Fig. 25) the relucent line (B) of the cornea, which represents

FIG. 24.

FIG. 25.

Bowman's membrane, can be traced to the tip of what may appropriately be termed the "relucent superficial limbal spur," S. This spur can occasionally be seen indicated in a vague way in many slit-lamp pictures, but it is seldom delineated with the precision and clearness that accurate work merits. It corresponds with the area so familiar in histological sections of the limbus region—in shape like a tall "wedge," having its apex where Bowman's membrane stops short, lying beneath the epithelium anteriorly, while posteriorly it accommodates itself on the face of the lamellated fibrous coat of the eye by causing a shallow indentation which narrows the total thickness of the fibrous coat here. On, and just in, the anterior face of this spur lies the visible limbal vascular plexus whose corneal and finest loops—those more usually empty than not—normally reach a level which corresponds with its tip. So the superficial spur represents in section an optically heterogeneous zone of tissue at the superficial part of the edge of the cornea. The extent to which the superficial edge of this spur in optical section is convexo-concave is variable in different individuals, being scarcely curved in some; but it will be noted that the epithelial surface "impact line" of light E continued towards the bulbar conjunctiva does not, in the case here drawn, bend much, but follows an even course in a manner corresponding with the interposition, between it and the face of the spur, (*a*) of a greater thickness of the epithelium and, as the line comes more in front of the sclera, (*b*) of sub-epithelial areolar tissue. The contour of the epithelial surface is slightly concave for a short distance below. The shape of the face of the focused "block" of light of Fig. 24 displays the contour of the face of the spur; this is also seen in Fig. 1. The average position, in the section, of a trabecula T, and of a basal epithelial crypt C, is also indicated in the section, Fig. 25, as well as the peripheral part of one form of the arcus senilis. It is the thin final part of this "spur" when seen by retro-illumination that contributes the main constituent of what is often spoken of as the "bedewing of the normal epithelium at the limbus." The physical properties of the normal surface-epithelium at the limbus justifying the term "bedewing" are so very slight that they can only just be detected by a critical and experienced observer, though with pathological bedewing it is otherwise. The "bedewing" of the limbus, *i.e.*, the appearance of imperfect transparency so easily seen by casual retro-illumination is commonly due to the optical properties of the not quite transparent thin part of the superficial limbal spur.

Sometimes over this spur, and also more peripherally on the conjunctiva, thin, sharp superficial lines are seen more or less concentric with the limbus. They look like cracks in the epithelial surface, but they are only narrow linear invaginations of the surface. They are more apt to occur in the elderly.

Deep Vessels visible at the Limbus

Two more vascular elements, deeper and not to be included with the superficial plexus, are sometimes seen at the normal limbus. Figs. 26 and 27 represent portions (L,L) of the temporal region of the limbus of the right and left eyes respectively of an

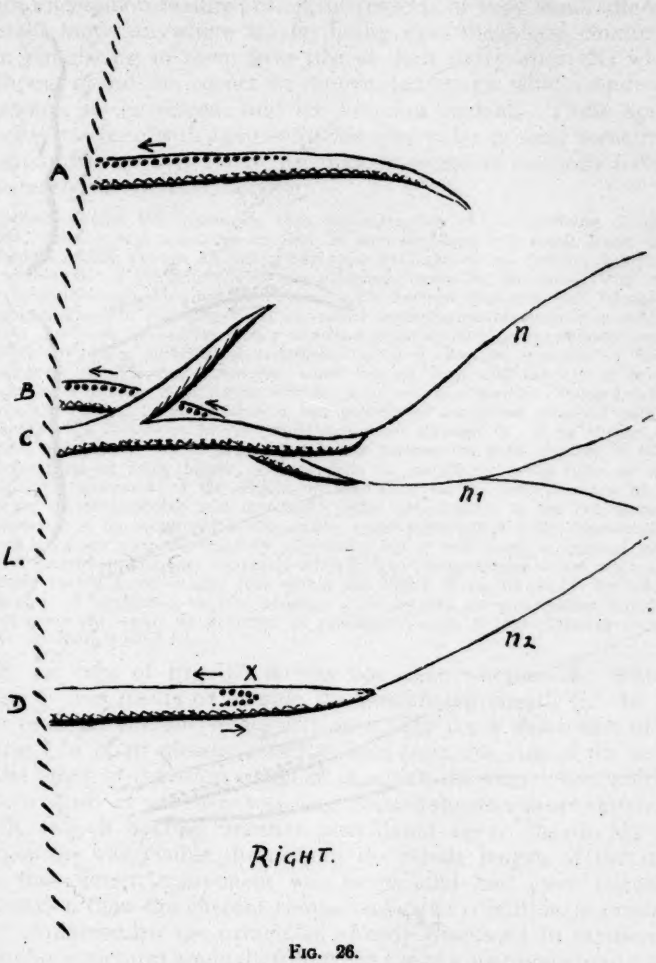

FIG. 26.

Medullary sheaths of the corneal nerve-fibres. The efferent component of a vascular loop is seen in both A and B. The tip of an afferent-efferent loop, X, is seen in D.

adolescent girl. They depict the peripheral medullated portions of nerve fibres so often noticeable about mid-way between front and back surfaces of the cornea at the limbus. If these short medullated sheaths are looked at carefully it will often be seen that each may contain one afferent-efferent fine vascular loop

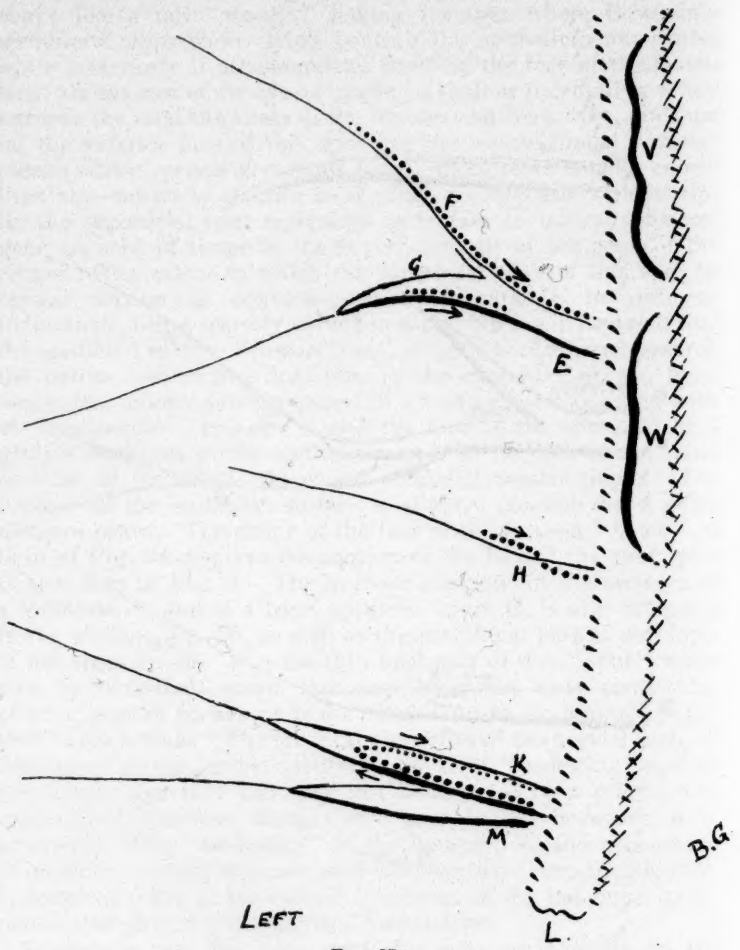

FIG. 27.

Nerve fibres (three, E, K and M, being medullated) and their associated vascular loops. V and W are deep, coarse vascular loops seen hazily in the depth of the limbus.

(shown by dotted lines). Usually, the afferent component is invisible and only the single efferent component is seen, as in A and B. (The medullated trunk C, in which no vessel is seen, overlies the trunk B. It may be remarked in passing that the asymmetrical manner in which the nerve, n, is seen leaving the end of its medullated sheath is accurately depicted.) D recalls a not uncommon feature; often, in respect of very small afferent-efferent loops anywhere in the living eye, the blood cannot be seen circulating in them save just at their sharp apex (X) where it shoots round the corner in interrupted spurts which render its existence, its movement and its direction evident. These spurts may be in phase with the cardio-vascular pulse or may sometimes be separated by irregularly attenuated successive intervals having apparently no such relationship.

(I often formed the impression that the perception of the *existence* of quick motion, when it was accessible to view in no more than very small areas, could be formed readily enough by direct inspection with the retinal fixation point; but that conception of the *direction* of the movement could be determined with more ease by deliberately viewing the feature with fixation displaced just enough to be perimacular. In recording rapid movement occurring simultaneously in different relative directions in minute closely crowded features only just resolvable—as in close-set developing pathological endothelial tubes—I used to encounter a fallacy of apparent simultaneous similarity, when looking long and intently at a very minute vessel in order to determine whether it served an afferent or efferent function, with nothing more to go by than a just perceptible occasional transient pulsatile spurt of a few corpuscles in very rapid movement through it. If by chance such a vessel had near it—so as just to fall in the perimacular field—another in which (perhaps from its being bigger, perhaps from its circulation being fuller or more regular) the movement of the circulation was more visible, then the view of this latter in the perimacular field dominated, often erroneously, in the conception of the *direction* of the movement in the smaller vessel perceived with the fixation point. It was a fallacy soon overcome by education; but it was prone to mislead me at first. I found it particularly noticeable when fatigued by prolonged visual and mental straining to see features only just within the limits of resolution, or by adverse conditions. I mention it—in the personal sense in case an idiosyncrasy may have played some part—only as a matter of passing interest; it plays little or no part in the instances quoted here.)

In the case of Fig. 27 it was not clear whether the efferent vessel F was inside or outside the medullated sheath E. In the case of G an efferent vessel was seen only for a short part of its course. In H an efferent vessel crossed from one side of the nerve to the other in the short distance in which the vessel was visible; as to whether or not there was a medullated sheath was not apparent. In K (which overlay another medullated nerve sheath M) the circulation was visible throughout the whole length of the loop and the afferent component was larger and had more leisurely circulation than the efferent component; this condition is presumably explained on the principles already discussed in relation to a similar structural anomaly formed in the conjunctival circulation. It may be remarked that, owing to the rather similar simple optical properties of the tissue of medullated sheaths and empty blood

vessels, the latter, when within a medullated sheath, can scarcely be distinguished when it contains no blood. But it will be noticed that in the two examples of vascular loops here quoted whose circulation renders their apices evident, the apex falls short of the end of the sheath. This is common, as also, if I remember correctly, is the numerical proportion of not more than one loop in one sheath. Speaking from memory, without searching my records, I do not recall having seen vascular loops accompanying fibres that are, as is more usual in the cornea, non-medullated.*

The second additional vascular feature referred to above is diagrammatically illustrated in Fig. 27, V and W. Its occurrence in this particular case is a chance one and does not indicate a relationship with the presence of medullated nerve fibres. It is in the form of one or two pink vascular loops, rather large both in calibre and extent, such as are sometimes seen hazily in the limbus jutting out from within the sclera and lying mid-way between the front and back surfaces of the corneal periphery. They are thus deep and have nothing to do with the vessels of the superficial limbus-plexus, compared with which they are much coarser. They are probably derived from perforating branches of the anterior ciliary vessels. They are by no means uncommon. I have not searched my notes for the records of them which are scattered here and there among stored-up records of other conditions, but as far as I recollect these loops were found more or less in the region of "3 o'clock" and "9 o'clock"; I do not recall seeing them above or below, but it may be added that the lids render these parts less accessible to casual inspection. However, I seem to recollect making a note of an anterior ciliary vessel which ran up to the limbus from below and then sank into the sclera to continue as a buried and only just visible loop from about "6.30 to 7.30 o'clock" deep in the limbus. It seems curious that such features do not occasionally reach into the cornea as a developmental aberration.

The Peripheral Post-Corneal Rim

Mention may be made of an ill-defined textural non-vascular zone of faintly increased relucency at the extreme periphery of the posterior part of the cornea depicted diagrammatically in the lower end of the deep face (P) of the corneal "block" (Fig. 1). It is not a constant feature and its visibility is faint. It commonly has some antero-posterior depth, especially at the extreme

* Meesmann in his "Spaltlampen-Atlas" says that I have found that the superficial part of the vascular corneal invasion, in interstitial keratitis, follows the paths of the nerves. I mentioned this in the *Brit. Jl. of Ophthal.*, October, 1924, p. 470, as being a possibility, but I did not then add that I had seen it in only two cases of interstitial keratitis.

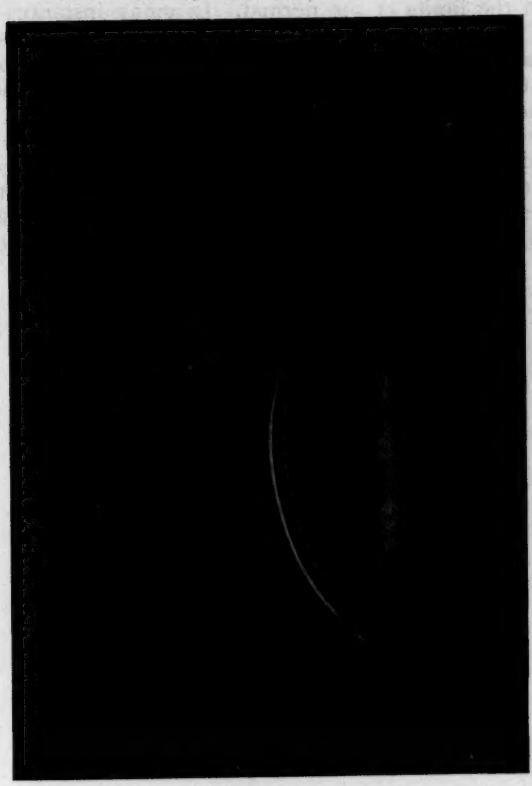

FIG. 28.

Peripheral refractile post-corneal rim.

periphery, but it is thin centrally, so that it is often somewhat wedge-shaped in section.

Attention may be drawn, in concluding, to a structural feature by no means uncommon which, schematically represented in Figs. 28 and 29, I have suggested might be named the "*peripheral refractile post-corneal rim.*"* Many years ago I collected numerous records of variations of this feature which was so common as to

*The visibility of the rim is exaggerated in the reproduction of both these figures owing to its having been drawn (as well as the initials in the corner of Fig. 28) with process-white. It may here be added that in Fig. 1 the stippled bedewing at the limbus has for the same reason come out unintentionally bright; in the coarseness suggested by this error it might be more reminiscent, in a purely diagrammatic sense, of a pathological bedewing. I did not foresee this when drawing these figures.

be within the limits of the normal. In many instances its form was very inconspicuous; when well marked it was, in the cases I saw, usually more in evidence on the temporal than the nasal side; its edge usually receded gradually from view behind the limbus above and below and it was seldom seen in the upper or lower limbus arcs. When present it was often, but not always, bilateral and its development was seldom symmetrical in the two eyes. Diagrammatic examples from two persons—for access to whom I am indebted to Sir Richard Cruise—are shown in Fig. 30. Quite rarely minute fragments of tissue, having a strong semblance to

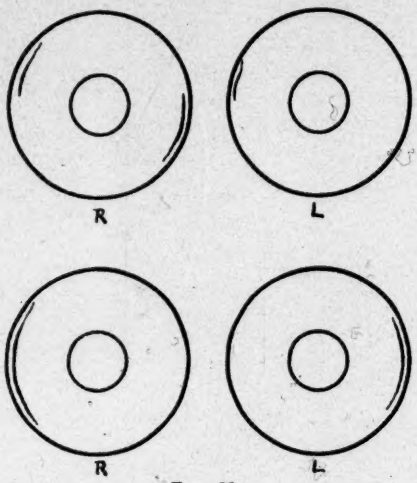

FIG. 30.

the tissue forming the stroma of the iris, were seen attached to, or close to, the edge of this rim. In Fig. 31, which shows the condition in a left eye, it was more pronounced on the nasal side N. (It was not present in the right eye of the same subject.) The gap G between the slightly spread ends, B and C, was very nearly 1 mm. wide; D represents the rim on the temporal side T, where the dotted line F represents the relative position, in this particular case, of a prominent normal circumferential fold of the iris.

Fig. 32 is another example. P depicts a small fragment of brown tissue on the back of the "rim" of the same colour (dark brown) as the stroma of the iris.

Fig. 29 is intentionally given as being schematic. It was recorded from the same subject as was Fig. 28 in whom the rim (at the edge M) was very conspicuously developed, but its representation in Fig. 29 as running in the form of an appreciable and

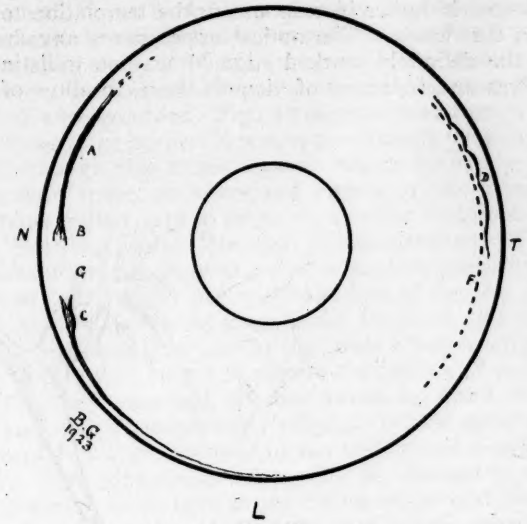

FIG. 31.

Linear magnification: approximately x 6.

FIG. 32.

thick relucent and transparent membrane right into the periphery of the chamber is rather in response to the temptation to forsake visible fact for fiction. The optical appearances anywhere peripheral to the definitely marked edge M are too indistinct, both in themselves and in access of view to them, to allow of definite

FIG. 33.

Linear magnification: approximately × 118.

interpretation. But it can be affirmed that in well marked cases the *edge* M is definite in its thickness (variable), its configuration (sometimes regular, often variously irregular, as in Figs. 31 and 32) and in its having optical properties indicating that it is a contour elevation towards the anterior chamber of higher refractive index than the aqueous fluid. In both Figs. 31 and 32 it is the conspicuous "thick edge" that has been drawn. Sometimes this edge was found to be just in line with the demarcation between

the main flat region of the iris and the small peripheral part of the iris-face which slopes back in the chamber angle to unite with the anterior end of the ciliary body; but neither this spatial alignment, nor one relative to the circumferential iris folds, seemed constant.

Less often, grotesquely-shaped and much smaller features of a like kind were recorded; Fig. 33 depicts one; from a to b was about 0·75 mm.; the portion X was approximately 0·6 mm. from the limbus L (though this raises a point, which cannot be discussed here in a short space, on where and whence to take measurements at the limbus region—apt to be so vague when magnified; various possible "starting points" are open to consideration). P indicates on the translucent adventitious tissue, a small fragment of material of the same colour (light brown) as the face of the iris.

These observations were made some 10 years ago under disappointing circumstances; but at that time I had a tangible hope of being able to find means to pursue the subject of the slit-lamp in detail for many years and, not then foreseeing that I should soon have to abandon it altogether, I tried to include detailed records of the normal in a preliminary to the anticipated continuance of the work. This communication is only an abstract from various records that were made then in the course of general observations on a very limited number of cases not particularly selected on this account. It is by no means exhaustive. The type of records chosen for reproduction are not difficult to make but some of the generalizations may, indeed, be digressive or untenable, and I would by choice have preferred to investigate much further the subjects discussed before writing on them. Nor has this report the accessory aid of any histological or physiological investigation and it touches on the fringe of interesting speculations merely from one view-point.

Turning back now to the discarded records of an abortive attempt, I would be cautious, in reviewing any condition included in them, to say it is a rare one; but the "peripheral post-corneal rim" was noted relatively so frequently that it may safely be called a common feature. It would seem possible that the "congenital hyaline membranes" on the posterior surface of the cornea described by Miss Mann in the *Brit. Jl. of Ophthal.*, August, 1933, may be an aberrant exaggeration related to this inconspicuous variable feature.

SENILE CATARACT—A STUDY OF THE BIOLOGY AND CHEMISTRY OF THE CRYSTALLINE LENS*

BY

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MANY diverse methods of approaching the complex subject of senile cataract have been used. Research into the control of the transparency of the crystalline lens and the development of opacities requires a working hypothesis. This paper deals with a joint consideration of the biology and chemistry of the crystalline lens, both in the normal and abnormal states and with an hypothesis of the development of cataract.

Outline

1. Growth and structural changes in the normally ageing lens.
2. Chemistry and nutrition of the normal lens.
3. Analogous changes observed in other cells and organs, especially cells of bradytrophic tissues. Changes in permeability in ageing cells. Rôle of calcium and lipoids in permeability changes. Hereditary factors influencing the ageing of an organ or part of an organ.
4. Discussion of cataract with formation of hypothesis of development of cataract.
5. Conclusions.

1.—Growth and Structural Changes in the Normally Ageing Lens

The origin and development of the crystalline lens.—The lens is of ectodermal origin. The human "Anlage," a thickening of the ectoderm after contact with the optic vesicle, is visible at the 15th to 18th day of embryonic life. The posterior cells of the lens vesicle differentiate into the primitive cortex. Further growth and formation of the lens fibres is accomplished by the cells of the vortex at the equatorial region. The anterior epithelial cells

* The material for this thesis was collected while Daniel B. Kirby was Research Fellow in Ophthalmology for the American Academy of Ophthalmology and Oto-Laryngology, and R. von E-Weiner was Consultant Research Chemist to the Department of Ophthalmology, Columbia University.

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probably divide, and move out radially to furnish cells for the vortex. It is here that the lens fibres are continually developed.

The crystalline lens capsule.—The embryonic cuticula is formed as a secretion or deposit by the lens epithelial cells and is developed into the lens capsule. The latter is a strong, glass-like, semi-permeable membrane, varying in thickness, being thinnest at the posterior pole. The adult capsule is formed by accretion from the inside layers of similar material produced by the lens epithelial cells. It is undoubtedly first in semi-liquid form and is forced under capillary pressure around and between the cortex and the previously existing capsule, fusing with the latter. This mechanism of formation explains the thinness of the posterior as compared with the anterior capsule. The degree and selectivity of permeability of the capsule are important factors in the health of the lens. The lens epithelium, which continues to form new cells throughout life, is present only under the anterior part of the capsule, and extends somewhat beyond the equator.

The crystalline lens epithelium and new lens fibres.—The anterior and vortex epithelial cells represent the only nucleated, reproducing elements in the lens. The young lens fibres, which lie at the periphery of the lens, have smooth edges, are rounded or ovoid on cross section and contain a nucleus. The nuclei of these fibres degenerate gradually, as their fibres are pushed toward the interior by the newly-formed fibres. The nuclei are first fragmented into small, intensely staining particles and then gradually disappear.

The crystalline lens cortex.—The crystalline lens cortex represents the softer, more recently-formed lamellae of lens fibres, the most recent being outermost. The younger fibres contain more water and the interfibrillar diffusion spaces are more open than those of the nucleus. The relative amount of soft cortex and hard nuclear material varies with the age and the individual tendency to sclerosis of the nucleus, either physiological or pathological. The fibres are six-cornered, flattened cells, and the older fibres have finely denticulated edges. The fibres may be pictured as flat tubules, which in the cortical portion of the lens are about 10 to 12 micra wide, 2 to 3 micra thick, while their length may be measured in millimetres. The interior of the fibres consists of a clear, rather viscous colloid substance, the lens protein. The lens fibres may be likened to red blood corpuscles in their structure, because of the absence of nuclei in the mature fibres and the apparent lipoid membrane. Between the fibres there is a cement substance which stains in the familiar way with silver nitrate.

The crystalline lens nucleus.—The crystalline lens nucleus represents the more dehydrated, hardened, older portion of the lens. The lens fibres, which in the advancing period of life have been

sub-capsular, are later pressed to the central zone. Formations, typical of various stages of development, may often be distinguished by their accretion boundaries, zones and sutures. The hardened nuclear formations develop irregularities of interfaces, pressure surfaces, colorations and refraction-index differences which may produce nuclear haze of beginning cataract.

Transparency of tissue.—The transmission of light through a perfectly transparent tissue is effected without scattering. This perfect transmission rests upon the structural organization of its constituent molecules, as well as the aggregation and direction of its micelles and cells. In the early embryonic state, the lens represents a sol and the dispersed phase with exhibition of Brownian movement of the micelles may be demonstrated with the aid of the ultramicroscope. In the later embryonic state the transformation of the sol to a gel takes place. In this process there may be a partial reorientation of the constituent micelles. The hydration of the proteins increases and in the mature lens most of the dispersion medium is firmly held by the lyophilic protein molecules. The concentration in unit volume is too great and the particles cannot be resolved by the ultramicroscope.

Weight and volume of the lens.—The weight of the human lens increases from an average weight of 0·175 gs. at the third decade to an average of 0·265 gs. in the eighth decade of life, an increase of over 50 per cent. Since the lens is a closed system, it must adapt itself to a more or less constant volume. This is only possible by a diminution in volume of the individual fibres. As the older fibres become more and more compressed by the steady addition of newly-formed fibres, there is a loss of fluid content and the fibres become increasingly sclerosed. This physiological hardening of the fibres cannot be compared to the formation of the horny layer of the epidermis. The chemistry of the two processes differs. The water content of the nuclear fibres of the lens and the soluble protein content is very much reduced in the ageing process.

2.—Chemistry and Nutrition of the Lens

Chemical constitution of lens.—The young adult lens consists of approximately 35 per cent. protein, 64·5 per cent. water, holding electrolytes and organic crystalloids in solution and 0·5 per cent. alcohol-ether soluble substances, sterols, lipides, fats and fatty acids.

Protein fractions of the lens.—The protein concentration of the lens is greater than that of any other body organ. There are two main fractions of the lens protein, a water insoluble fraction called albuminoid, and a water soluble fraction. The latter com-

bines alpha-crystalline, beta-crystalline and gamma-crystalline. The gamma-crystalline, which has been isolated from the beta fraction, constitutes the total albumen content of the lens.

Protein changes in the normally ageing lens.—The relative concentrations of the two main fractions, as well as of the crystallines, change with age. For cattle lenses the ratio of soluble protein to insoluble protein changes from an initial 77 : 23 in the lenses of calves five weeks old to 41 : 59 in the lenses of 16 year old cattle.

Weight and water content of the lens.—The total weight of the lens increases with age. For cattle lenses the increase is from an initial weight of 0·91 gs. to a final weight of 2·7 gs. The total protein content increases from 32 per cent. (0·29 gs.) to 37 per cent. (1·0 gs.) There is therefore an absolute and a relative increase in protein content with age. Likewise, there is an absolute and relative increase in electrolytes and lipoids. The increase in water is only absolute; relatively the water content decreases with age. Thus the water content of cattle lenses decreases from a concentration of 76·4 per cent. (0·614 gs.) to 62·6 per cent. (1·9 gs.)

Lens protein fractions.—The shift in the ratio between soluble and insoluble protein fractions has been attributed to a transformation of the protein. This is rather difficult to reconcile with the established variations in concentrations of the amino-acids constituting the proteins of these groups. Whether the pressure, lack of nutritive and respiratory facilities to which the central fibres must be subjected, are sufficient to bring about such far reaching reconstruction or changes in the protein molecule, remains a matter of speculation. Loss in solubility does not necessarily demand a change in constitution, but may be brought about by the formation of stereo-isomers, that is, a change in the configuration of the protein molecule.

Isomers of the lens protein molecules.—The opportunities for isomeride formation of a protein molecule are almost unlimited. It has been postulated that the infinite variety of forms found in organic nature is partly the result of isomerism of the protein molecule. Assuming the presence of 15 asymmetric carbon atoms in any of the soluble protein of the crystallines, the possible stereo-isomers of that protein are ^{1} or 32,768 in number. To this must be added the further possibility of tautomerism in the $-C^{O}_{NH_2}$ group of the amino-acids. This group may assume the tautomeric form HO - C = N—and thereby give further opportunity for isomerism. A change in the structural formula may bring about loss in absorbing power for solvent, dehydration, exposure to enzyme action, change in state of aggregation, etc.

Hysteresis of the lens proteins.—The changes which the epithelial cells undergo in their gradual transformation into peripheral and later, nuclear fibres, will produce an hysteresis effect on the

chief lyophilic constituent of the fibres, the proteins. The term hysteresis expresses the divergent behaviour of a colloid solution due to its previous treatment. The initial treatment of a protein solution may change certain of its physical properties, chiefly its solvating ability and solubility.[1]

Plasticity of lens protein.—Aside from the forces inherent in the progressive development of the lens, time itself has an effect on the viscosity and plasticity of lyophilic colloid solutions. The ageing of a colloidal system, such as a protein solution, seems to be accompanied by a decrease in its solvating properties and a consequent decrease in viscosity. The gradual transformation to a more stable isomeride producing the sclerosis of presbyopia may be due to the ageing of the protoplasmic proteins. It may be that a gradual fixation of a more stable form initiates age changes and prepares for the ultimate death and subsequent resolution of the cell to its constituent elements.

Other Chemical changes.—The effect of a gradually increasing electrolyte concentration, especially calcium, and the increase in concentration of the ether soluble constituents, on the physical state of the proteins must also be taken into account. To this must finally be added the cumulative effect of the products of lenticular metabolism, and the diminished rate of clearance of these products with increasing age and decreasing permeability of the lens and capsule.

Free and bound water.—Though the decrease in water content of the aged lens has been frequently demonstrated, there are so far no analyses of the free and bound water of the lens, and changes in the ratio of free to bound water which develop with age. A shift in the ratio in favour of free water may be assumed from (1) the known effect of age on the water binding capacity of protein, (2) the increase in calcium, fatty acids and sterols, (3) physical appearance of aged lenses.

Inorganic contents of the lens.—Coincident with the relative decrease in water content of the aged lens, the electrolyte concentration is increased. The ash of the lens increases from an initial concentration of 3 per cent. to approximately 3·8 per cent. This increase is mainly in the calcium and phosphorus. The calcium increases 15 per cent. of its initial value and the phosphorus 26 per cent. Part of the increase is derived from organic compounds of these ions.

The capsule has been reported as freely permeable to electrolytes. O'Brien and Salit[2] report the chloride concentration of the ox-lens as averaging 356 mgs. per 100 gs. of wet material. The concentrations reported for the aqueous humour and vitreous by these authors were 709 mgs. and 681 mgs. per 100 gs. of material. This difference is considerable, even if the reduction in soluble space

in the lens is taken into account. It would be interesting to determine the chloride content of calves lenses. In how far the demonstrated increase in cholesterol of aged lenses plays a part cannot be definitely stated. However, it is known that cholesterol decreases the ability of a tissue, other than the liver, to hold chloride.

Most important from the standpoint of permeability and solubility of the lens protein is the reported increase in calcium. Calcium crystals have frequently been found present in the nuclei of normal lenses, obtained post-mortem from patients above 50 years of age. Such crystals were not found in younger lenses. [3]

Horning and Scott[4] have shown that the distribution of inorganic constituents changes during the gradual development of the embryonic chick lens. "The calcium accumulates along the inner cavity of the lens, the iron salts appear to have migrated toward the periphery." This finding suggests the probable value of further work on the mineral skeleton of the lens at various ages, by the micro-incineration process of Policard[5] and of Scott and Horning.[6]

A shift in the relative concentrations of potassium and calcium in the growing eye has been demonstrated by Kaufman and Laskowski[7]. The calcium concentration increases and the potassium concentration decreases with age. The reduction in the K/Ca ratio parallels the rate of growth. However, this phenomenon may also be an expression of the increasing sclerosis. If, analogous to the red blood corpuscles, calcium does not infiltrate the fibre, whereas potassium does, and is largely present in the interior only, then, as the ratio of volume to surface of the fibre decreases, the ratio of potassium to calcium must also decrease.

Organic constituents of the lens—glucose.—Among the organic metabolites, the glucose content of ox-lenses has been determined by O'Brien and Salit[8] as 134·7 mgs. per 100 gs. of wet material. This is in excess of the glucose content of either aqueous humour (average 87 mgs.) or vitreous (average 56 mgs.) also determined by these authors. Part of the glucose content of the lens may have resulted from autolytic breakdown of cellular carbohydrate material. It may also be due to the presence of other reducing substances, such as glutathione in reduced form.

It has been calculated that the eye uses 438 mgs. glucose per day and that the oxygen available suffices for 200 mgs. only. The rest of the glucose is said to be broken down to lactic acid. The glucolytic breakdown of glucose within the lens is also indicated by the presence of lactic acid in the aqueous humour in greater concentration than in the blood plasma. Furthermore, Kronfeld and Bothman[8] in their experiments on the oxygen consumption of the surviving lens have shown that the lens, *intra vitam,* has an

insufficient oxygen supply and has the property to glucolyse glucose under aerobic conditions. The surviving lens shows a minimal oxidative and quite marked glucolytic metabolism of carbohydrate material. Determination of glucolytic activity of sections of sterile cattle lenses by Michail and Vancea[9] showed the activity of the cortical layer to exceed that of the sclerosed nucleus.

Lactic acid.—The lens in its capactity for lactic acid formation resembles a tissue cultured *in vitro* in which 40 per cent. of the total glucose consumed is converted to lactic acid only. The transient influence of the lactic acid on the lens protein should be recognized, even though the acid is promptly neutralized by lactate formation. The lactic acid radicle has a swelling influence on protein.

The auto-oxidation mechanism.—The lens possesses no circulatory system. It is surrounded by the intra-ocular fluids. For its nutrition as well as oxygen supply it depends entirely upon diffusion processes. Means for the conservation of the available oxygen supply are present in the auto-oxidation-reduction system of glutathione, thermo-stable reductor. It has been shown that glutathione is present in the lens and that it may be extracted with water or dilute acids, without hydrolysis of the proteins. Glutathione is a tri-peptide, glutamyl-cysteil-glycine. In the reduced form it contains a free sulphydryl group. Compounds containing this - S - H group are important in tissue respiration and intracellular oxidation. The sulphur in this state readily undergoes partial oxidation to form the di-sulphide (- S - S) compound. In the presence of reducing substances this compound is again converted to the sulphydryl (- S - H), mono-sulphide state. In order that the glutathione may function as an auto-oxidation-reducing system, normal alkalinity of the lens protein and tissue fluid is essential.

Sulphur is a constituent of the soluble protein of the lens. The beta-crystalline fraction is richest in sulphur. However, in the protein molecule the sulphur is either present in the oxidized form or the sulphydryl group is protected from reacting since the lens from which the glutathione has been extracted no longer gives the reaction with sodium nitro-prusside, the qualitative test for the S - H group.

The term "oxidation" is rather unfortunate as it seems to imply the actual participation of the element oxygen in the reaction and is therefore often confused with combustion. Chemically speaking oxidation ultimately means the assumption of a positive charge or the loss of a negative charge by an ion or atom. Every oxidation reaction involves a simultaneous reducing reaction. Viewing the oxidation of the sulphur in the cysteine radicle of glutathione from this standpoint will serve to clarify the relation of glutathione to

the inner respiration of a tissue. Glutathione may be determined quantitatively by titrating its solution with a solution of molecular iodine. In this action the sulphur atom, which is negatively charged, is partly oxidized and the di-sulphide is formed. The iodine as the oxidizing agent is reduced to the ionic state and acts as the hydrogen acceptor. Likewise glutathione in the oxidized state may bring about oxidation of a compound by acting as hydrogen acceptor and being reduced to the sulphydryl state. The glutathione does not furnish oxygen for the combustion of sugar or other metabolites. It acts as a catalyst by forming the di-sulphide compond in the presence of molecular oxygen. In this state it acts as an hydrogen acceptor or in other words as oxidizing agent. In this respect it may be said to conserve oxygen, as it acts the part of the oxygen in the removal of the hydrogen. Since the oxygen supply is limited, the presence of such a compound as glutathione becomes important.

In the ageing lens the concentration of glutathione in the sulphydryl form is lessened. This would be in accordance with the decrease in oxidative processes within the lens substance, due to the increasing sclerosis of the lens fibres and decreasing vital activity.

The stimulating action of glutathione on cell proliferation has been demonstrated. Hammet and his co-workers have shown that the -S-H group is the essential and natural stimulus to cell division.[10] The question thus presents itself as to how far a depletion of the sulphydryl compound of the lens effects the physiological maturing of the lens fibres.

Enzyme action in the lens.—Enzymes capable of accelerating oxidative processes are present in the lens as well as in the intra-ocular fluids. The presence of oxygenase, peroxidase as well as catalase has been demonstrated. These three enzymes represent a completely functioning oxidative system.

No systematic determination of the enzymes present in the lens has thus far been carried out. La Coscia found lipase, amylase, oxidase, catalase and glucolytic enzymes in the aqueous humour and in the vitreous. He also determined the presence of protease, catalase and lipase in the lens.[17] Hayana determined the presence of proteases in the aqueous humour.[18] The presence of these enzymes in the lens is likely. There may also be present phosphotases, which are said to be present in epithelial cells, as well as lecithinases, which are quite widely distributed.

Hydrogen-ion concentration of the lens.—The hydrogen-ion concentration, the pH of the lens has been determined potentiometrically by Scalini.[11] The average pH of the lens was found to be 7·38. It lies, therefore, within the range of the pH variations for the aqueous humour, determined by Yudkin as 7·32 to 7·55.[12]

The normal pH range of venous blood plasma ranges from 7·33 to 7·55. Like other tissues, the normal lens maintains its pH within narrow limits.

*The lipoids of the lens.**—The lipoids of the lens increase with age. The cholesterol content of the normal young-adult lens approximates that of the blood, *i.e.*, 150 to 160 mgs. per 100 gs. of wet tissue. In old age this concentration may be more than doubled. Goldschmid extracted human lenses post-mortem with various organic solvents and studied the lipoids in the various fractions. The cholesterol was found to increase markedly from birth to the end of the second decade. This is followed by a slight decrease during the next three decades and a subsequent rise in the seventh decade. The phosphotide fraction decreased during the first two decades and then increased slightly, but never exceeded the concentrations found during the first few years of life.[13] There is a distinct shift in the relation of cholesterol to phosphotide in favour of cholesterol. Such a shift in ratio is of great importance from the point of view of cellular permeability and metabolism. G. Schlombke[14] found the cholesterol content of cattle lenses to increase from 196 mgs. per 100 gs. of wet material, during the first year of life, to 608 mgs. for aged cattle.

The sterols, cholesterol and its esters, are negatively charged, hydrophobic colloids. They are adsorbed on the cell surface, render the cell less permeable and isolate it electrically. According to Burger[15] organs little or not at all supplied with capillaries are most easily impregnated with cholesterol. The lipides, on the other hand, are lyophilic colloids and have great swelling capacity. It has been shown that while cholesterol depresses cellular respiration, the phospholipin, lecithin, may act as oxygen carrier and have a stimulating effect on the inner respiration of a tissue. While the sterols in the environment of tissue cells and fluids have a physical function like all lipoids, the influence of sterols on cellular metabolism is much less marked than that of lipides. It seems that the fat metabolism of an organ is related to its phosphotide content and organs with a high fat metabolism also have high phosphotide content. Cholesterol, on the other hand, may retard fat metabolism. It inhibits lipase action probably by adsorbing the enzyme.

Among the vitamins of lipoidal nature vitamin A is present in the retina in relatively large concentration. Whether this vitamin is also present in the lens has not yet been determined.

Factors influencing the surfaces of the lens and its cells.—One may picture the cell surface as a mixture of proteins and lipoids.

* Lipoids are organic compounds, soluble in ether or other organic solvents. The group includes (1) Sterols, *e.g.*, cholesterol. (2) Lipides, *e.g.*, lecithin, sphingomyelin. (3) Cerebrosides, *e.g.*, phrenosis. (4) Neutral fats, fatty acids and soaps.

It is due to the proteins and hydrophilic lipoids present that the cell is permeable to water and dilute salt solutions. Owing to the colloidal nature of this protein-lipoid membrane, calcium exerts a permeability decreasing action. Potassium, by its peptizing influence, increases the permeability. The younger a cell, the less stable the formation of the surface layer and the more permeable the cell. Chambers showed that the membrane of a cell, as demonstrated by micro-dissection, has not a static, but a constantly varying structure. It can repair injury and the film, newly-formed, attains a certain rigidity through accumulations outside and inside of the cell. Calcium is necessary for the formation and maintenance of the membrane.[16]

With increase in cholesterol and calcium concentrations and the gradual breaking-up of the nucleus the lens cells become less and less permeable, the membranes assume a more and more unchanging character. The film thickens, the rate of exchange between interior and environment is decreased, until finally the isolated state of fibre is reached.

3.—Analogous Changes in other Tissues

The nutritive requirements of the tissue cell are supplied by the environment. Those cells which possess the best nutritive provisions will maintain themselves at the expense of the others, less well provided for. To the lack of nutritive material for the cells in certain parts of a given tissue must further be added the lack of adequate excretion and secretion. The same holds for the cell as such. The nucleus and the central part of a cell are the first to suffer from lack of nutrient material and insufficient removal of waste products. The resulting accumulation of catabolic material and cellular detritus initiates the ageing of a tissue. From time to time this excess, instead of being destroyed, is rejected in the form of a necrosis. The formation of such a "Nekron" is regarded by Kotsovsky as the beginning of age and death, as the death germ.[19]

The structure of the lens renders it especially vulnerable to age changes. The lens relies upon diffusion processes, the surrounding ocular fluids supplying nutrient material and removing waste products. The conditions in the central part of the lens differ widely from those prevailing in the peripheral parts.

In the lens the fibres gradually lose their nuclei. The nuclei are first broken into fragments and these gradually disappear. Since the character of assimilation is determined by the nuclear apparatus, the aged lens, in which the ratio of nucleated fibres to non-nucleated fibres decreases, must show a gradual weakening

of its metabolic processes. Waste pigment may also accumulate in the aged lens. The change in colour of the lens may be due partly to the greater consistency of the proteins and partly to waste pigment formation.

Chemistry of ageing.—The chemical processes of the physiological ageing of a tissue may be divided into:—(1) Primary changes; loss of water, thickening of substance, decrease in permeability, changes in diffusion. (2) Secondary changes; deposition of organic and inorganic waste material, accumulation of pigment, accumulation of sterols and fats.

Changes in bradytrophic tissues.—Burger and Schlombke[20] chose bradytrophic tissue for the investigation of the chemistry of the ageing process. Bradytrophic tissue is that which has little or no supply of capillaries, such as certain layers of the aortic wall, cartilage, the sclera of the eye and in a certain sense, the ear drum. Such tissue shows significant age changes. Bradytrophic tissue in its uniformity of structure, resembles a non-living colloidal system more closely than other tissue. One may, therefore, expect to find certain analogies between the chemistry of the ageing process of such a tissue and the gradual transformation of a sol to a gel and the subsequent gradual loss in water binding capacity of the gel on ageing. Burger and Schlombke found the dry substance of human cartilage to increase from 24 per cent. in the first decade of life to 42 per cent. in the seventh decade. The changes in cholesterol concentration determined for human cartilage are analogous to the changes determined by Goldschmid for the lens. In both these tissues there is a rapid rise in cholesterol concentration during the first three decades of life, followed by a slight drop and a subsequent rise in old age. Both human cartilage and aorta show a close analogy in changes in water content, calcium and cholesterol to those of the ageing lens.[21] Increasing dehydration was also shown for skin and sclera. The dry substance remaining after the evaporation of water changed in the sclera from 14·6 per cent. to 18·7 per cent.; in the skin from 28·6 per cent. to 35 per cent. of the original weight. In the lens the dry substance increases from 23·8 per cent. of the total weight to 37·4 per cent.

Loss of water, increase in calcium and cholesterol are primary changes in bradytrophic tissue, whether of ectodermal origin like the epidermis, lens or sclera, or of mesodermal origin like the aorta or cartilage.

The calcium and cholesterol concentrations of the blood are usually somewhat increased in old age. The cholesterol increases from an average of 142 mgs. per 100 ccm. of blood to an average of 182 mgs. Calcium also increases about 15 per cent. above its average value in early middle age. High cholesterol-ester

content has often been found associated with tissue degeneration. The chemical disorganization of the lens fibres is often characterized by the appearance of anisotropic substances. (Jess[22].)

There is a close parallelism between phosphotide content and mitochondria content of a tissue. Mitochondria plays an important part in the physiological activity of the cell, and cells physiologically active have a relatively high lipide content. (Cowdry[23].) In the ageing lens the phosphotide content of the lens is decreased relative to the sterol and fatty acid content.

The signs of age in cells and tissues.—The signs of ageing tissue may be summarized as follows:—(1) Gradual dehydration, loss of water binding capacity, loss in permeability and changes in diffusibility. (2) Diminished metabolism. (3) Accumulation of waste material, incomplete recovery from fatigue. (4) Pigment formation. (5) Increase in sterol and calcium content. (6) A relative decrease in lipide content. (7) A possible decrease or loss in unsaturated fatty acid content. (8) A possible change in the configuration of the mineral skeleton of the cells.

The ageing process.—The ageing process is initiated as a local change and gradually spreads to the entire organism. Senile degenerative phenomena are homochronic. The separate organs and tissues follow in different forms a single law of ageing. Inheritance factors play a part in the difference in duration of life in individuals and species. In the same manner inheritance factors may play a part in the heterochronic ageing of an organ and the appearance of senility changes.

4.—Discussion of Cataract

Hypothesis of genetically determined cataract.—The genes are considered the carriers of inheritence factors. Their activity may be said to be due to certain specific areas, where the outwardly directed fields of force form an electric mosaic. The specificity of the gene depends not only on the chemistry of that particular area but also on the structural arrangement of the atom, molecule or ion in that portion. Any change in the solvent will register its effect not only on the configuration of the gene, but also on the molecular units coming within its jurisdiction. (J. Alexander 24.) The normal functioning of the genes therefore would demand the maintenance of the environment and an adequate supply and rate of removal of metabolic products.

Vogt maintains that the lens fibres are vitally differentiated and that their early or later degeneration is determined germ-plasmatically and inherited from generation to generation.[25] The majority of the lens fibres have no nuclei; and vital differentiation may

consist in a structural change of one or more of the protoplasmic components, imposed upon it by the genes, before destruction of the nucleus. The gene may have imparted a lasting effect on the electronic complexes, atoms, molecules and micelles in the environment. Pathogenic genes proteins may impart certain characteristics, which may render the lens fibre on absorption vulnerable to degenerative changes, dehydration, and the attack of proteolytic enzymes. If this hypothesis is tenable, then the tendency to senile cataract formation may be bestowed upon the lens fibres by the parent cells.

Structural changes in the lens in senile cataract.—For the purpose of this discussion, senile cataract may be divided into the hydrating type (senile cortical, posterior cortical, anterior and posterior subcapsular cataract) and into the sclerosing type (nuclear cataract).

Cortical cataract.—The early stages of the cortical types are characterized by a slight excess of fluid in the form of vacuoles, water-split sutures, separated lamellae, and ill-defined cortical haze. The fluid tends to follow certain lines of cleavage, both anterior and posterior, so that symmetrical areas are involved. Whether the fluid responsible for these phenomena is extruded from its combination with the lens protein or brought in through the capsule in excess of the normal amount is unknown. It is certain that in the later stages excess fluid is attracted through the capsule. The ill-defined haze in the cortex may be due to a cloudy swelling of the lens proteins within the fibres or to a lysis of the fibres with laking of the resultant fluid. In some instances it may simply be an oedema without any actual denaturation of the lens protein. The latter conception may explain the transient changes in the vision of some patients when the observer is unable to detect any change in the physical appearance of the vacuoles, split sutures or separated lamellae. Increase of the number of vacuoles, separated lamellae and split sutures marks the progress of cortical opacities. Greyish Morgagnian globules formed by the coagulation of the clear, colloidal fluid may develop. They are found in the split sutures and in the lakes of broken different stages of protein lysis, mixed with inorganic salts, sterols and fatty acids. At this stage the lens becomes swollen or intumescent. In the final stages the rapid death of the lens in shown by the autolysis of the fibres and proteins. Much of the material then goes into solution and is filtered off through the lens capsule. The lens which has been swollen then regains its normal size. The hypermature stages of the shrunken and Morgagnian types are produced by further digestion, extrusion and absorption of fluids and also by deposit of extraneous material.

The concentration of lipoids is greatly increased in cataract. In the cataractous lens fatty degeneration probably follows abnormal fat infiltration, due to reduced oxidation processes. With the beginning of the degeneration of the fibres, this becomes true fatty degeneration. The double refractive bodies may also result from substances released by the degenerating fibres through enzymatic processes. The excess of cholesterol and fatty acids present would promote the formation of such double refracting bodies.

Physiological and pathological nuclear sclerosis (presbyopia and nuclear cataract).—In the physiological-nuclear sclerosis producing the familiar presbyopia, the process is smooth and there is no essential loss of transparency or change in the essential dioptric focus of the eye for distant vision. The colour of the lens by incident light is that of a very light grey, the lens being more relucent than in youth. In pathological-nuclear sclerosis, the process is uneven and lenticular myopia or second sight develops. A nuclear haze is seen by transmitted light, and a coloration develops which is amber in the early stages and goes through the reddish hues even to the formation of the brown or black cataract. The loss of nuclear transparency may be due to physical changes—irregularities of the interfaces, pressure surfaces, or to chemical changes in the nuclear material. The clinical appearance of nuclear cataract is that of hardened, compressed fibres with diminished water content. The nature of the chemistry of the cataractous lens particularly of the nuclear type is similar to that of the normally ageing lens but greater in degree. The reduction in soluble protein content as well as the concentration of insoluble albuminoid is much increased. The cataractous lens loses its glutathione in whole or in great part. This parallels the decrease in inner respiration.

The numerous theories of the pathogenesis of senile cataract may be divided into four groups:—

(1) Functional, *e.g.*, excessive accommodation, due to uncorrected errors of refraction.

(2) Biological, *e.g.*, unequal sclerosis resulting in the separation of layers adjacent to the nucleus, decrease in regenerative processes of lens epithelium.

(3) Chemical, *e.g.*, faulty nutrition due either to decreased permeability, metabolic disease or arterio-sclerosis, damage due to toxins or toxic catabolic products circulating in the blood, absorption of infra-red or ultra-violet rays, abnormal hormone or enzyme influences.

(4) Genetic, *e.g.*, senile cataract being considered as the heterochronic appearance of one of the senile degenerative phenomena.

The theory which regards senile cataract merely as an expression of early senility in the eye suffers from generality. Yet if one compares the chemistry and the structural changes of the normally ageing lens with those of certain types of cataract, one is impressed with the similarity of many changes, which qualitatively are alike and differ only quantitatively. Various factors such as starvation, insufficient oxygen supply, nervous influences, toxins or enzymes may initiate the changes which prepare cells for their dissolution. It is difficult to limit the aetiology of senile cataract formation to a single factor or to a group of factors. Changes in permeability of the capsule, of the lens fibre membranes, changes in diffusion in the fibres and in the interfibrillar spaces, changes in water binding properties of the lens protein, early loss of vital parts of the cells, abnormal infiltration with fat and with inorganic material may all play an important part in initiating a cataract.

The protoplasm of the lens fibres may bear the imprint of its genes in the structures of component molecules, atoms and micelles. The structural configuration of the proteins of the fibres derived from mother cells with pathologically altered genes may be such as to offer little, if any, resistance to proteolytic intra-cellular enzymes, or to the infiltration of lipoids. If, in addition, there is a local autochthonic factor for promoting the deposition of lipoids the stage is set for the beginning of the cataractous changes. If the constitution of the fibres is such as to confer upon it susceptibility to these changes which are able to produce opacity because of a weakening of the cellular or protoplasmic resistance, then cataract may be viewed as germ plasmatically determined.

Such a condition may be brought about either by hereditary weakness in the genes or by changes in the environment, which in turn weaken the genes. In this way one may explain the earlier occurrence of cataract in patients with hormonal and nutritional deficiency diseases or with diabetes mellitus. In this hypothesis concerning senile cataract formation, the primary change is a genetically induced change in the structural configuration of the protein molecule. The genealogy of senile cataract families may be difficult to work out due to variations produced by environment, but the hypothesis merits consideration.

5.—Summary and Conclusions

A study of the development, growth and structural changes, chemistry and nutrition of the normal lens in its relation to the aetiology of senile cataract is presented.

Analogous age changes in structure and chemistry of bradytrophic tissue are reviewed.

The structural changes observed in senile cataract and the chemistry and nutrition of such lenses are discussed.

The theory which considers senile cataract germ-plasmatically determined is elaborated upon. Pathological changes in the structural configuration of the lens protein molecules predispose to a lack of resistance of the lens as an organ, to changes in permeability, to changes in water binding power and to fatty degenerations. These have an effect of promoting degenerative phenomena of denaturation, coagulation, and precipitation of lens protein and of inducing abnormal infiltration of fat and deposition of inorganic material. This hypothesis considers senile cataract to be a genetically induced change in the structural configuration of the lens protein molecule which makes it susceptible to the physical and chemical phenomena concerned in the production of cataract.

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VARIATION AND REFRACTION

BY

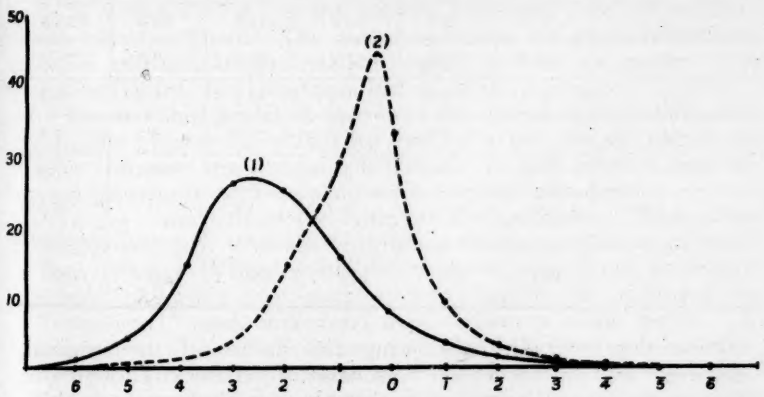
W. R. DUNSTAN

LEWES

MORE than 20 years ago Steiger developed his doctrine that myopia is not necessarily pathological in origin; but that a proportion of myopes arise simply as variations in growth. Unhappily, it has been assumed that if frequency distributions of refractive error be restricted to cases showing no pathological element then such distributions will follow the normal curve of error. This assumption having been repeated from author to author, it will be as well to deal with the matter of curve-fitting at the outset. In the first place the word "curve" should be reserved strictly for curves fitted by mathematical process. It has been—and still is—applied to frequency *polygons, i.e.,* graphical records of actual distributions, which merely put into picture form the frequencies found by the observer for successive values of the character under observation. To give completeness to the picture the tops are joined by freehand; but, in point of fact, such graphs are but a succession of uprights. When, however, the tops are joined peaks appear exhibiting the "roughness" of the original material. Moreover, the peaks vary from sample to sample. Now although the original graphs possess no mathematical properties yet it is found that if the samples are summed and, in addition frequencies are obtained for intermediate values of the character; then the polygon becomes smoother and, with each gain in smoothness, approximates more and more closely to a *curve*. Finding the curve by increasing the data is a process not only exceedingly laborious but, in most instances, impracticable. The statistician has to do what he can with the material at his disposal and it becomes his business, therefore, to find a suitable formula which will represent the original statistics as nearly as possible. This formula is the fitted curve. It *is derived from all the original data,* it represents the whole series by a few numbers (the constants in the formula), it facilitates comparison with results obtained by other observers and enables the statistician to supply missing terms.

Now the binomial curve was so derived from the data yielded by experiments conducted in the simpler cases of artificial chance; such experiments (for example) as the throwing of dice or the tossing of coins. Theory predicted it and experiment verified it. We may, if we choose, regard the occurrence of refractions as so many throws of nature's dice, but it is quite unwarrantable to

assume that the dice are not loaded. There *are* biometric distributions which approximate to the binomial curve but they are far from common and it is an exaggeration to say (as Brown and Kronfeld say) that "many a phenomenon" in nature can be represented by the binomial curve. Nor is it true to say that deviations from this curve are regarded as "indications that the material is not homogeneous." Again, the statement that "in the majority of instances an asymmetrical frequency curve should be interpreted as including at least two biological types" is also without foundation. The upholders of the binomial doctrine have published frequency polygons of refractions with superposed binomial curves; these being drawn on so small a scale that the asymmetry of the polygon is not immediately apparent. Now to endeavour to determine symmetry by inspection is simply to demonstrate that the eye, like the heart, is deceitful above all things. An overwhelming majority of biometric distributions yield a moderately asymmetrical curve and refractions are no exception to this rule. The measure of this asymmetry is called the skewness. Clearly the more nearly this skewness approaches zero; the nearer the curve is to symmetry. I have fitted curves to six frequency distributions of refractive error from various sources, including three that have been published as exemplifying the binomial symmetry. They all fall into the asymmetrical category; the skewness of each being definite. Two of these, representing the highest and the lowest, are shown in the graph; the chief characteristics being given in the table. In order to facilitate comparison the number of observations in each case has been reduced to 100, thus allowing the successive ordinates to be given as percentages.



(1) Board of Education Data. Children.
(2) Scheerer's Data. Adults.

CURVES OF REFRACTION

	(1)	(2)	(3)	(4)	(5)	(6)
Observer.	Wibaut.	Sorsby	B of E.	Wibaut.	Scheerer	Brown
Material (age) -	New Born	4–8 years	4–15	Adolescent	Adult	Adult
Number - -	2398	672	2624	2920	12000	4431
Type - - -	I.	IV.	IV.	IV.	IV.	IV.
Mean (D) - -	+2·6	+2·26	+2·28	−0·3	+0·3	+0·7
Mode (D) - -	+1·25	+2·31	+2·63	+0·2	+0·21	+0·61
St. Deviation (D) -	1·47	1·23	1·75	1·64	1·13	1·97
Skewness - -	−0·92	+0·04	+0·3	+0·3	−0·08	−0·05
Modal Ordinate -	30·2	40·0	28·2	32·1	43·8	27·0
+6 etc.	4·6	0·9	2·2	—	—	1·0
+5	7·2	2·3	4·7	—	0·3	2·0
+4	12·8	9·5	13·7	0·2	0·7	4·7
+3	15·7	26·7	26·2	1·0	3·4	6·7
+2	27·5	33·5	26·0	6·4	14·1	17·0
+1	29·8	19·0	15·1	23·3	28·3	19·0
0	1·9	5·7	6·8	31·7	33·0	25·8
−1	0·3	1·6	2·9	20·3	8·4	11·9
−2	0·2	0·4	1·2	9·5	1·5	8·0
−3	—	0·3	0·6	4·1	0·2	2·1
−4	—	0·1	0·3	1·8	0·1	1·3
−5 etc.	—	—	0·3	1·7	—	0·5
	100·	100·	100·	100·	100·	100·

Now these curves, considering the nature of the original material, are, on the whole, reasonably good fits. Though the data do not possess homogeneity they are none the less comparable. Without entering too deeply into statistical refinement it may

be said here that the Pearsonian system of curves consists of three main types, all of which are bell-shaped curves and possess skewness. At their adjoining frontiers are the subsidiary transitional curves which do not concern us. The three main types are known as I, IV and VI, the two former being represented in this series; though five of the six are of the same type, namely, type IV. The only representative of type I (Wibaut's new-born distribution), deals with data formed by pooling the observations of four observers. This frequency distribution was submitted by Wibaut as an example of a binomial distribution! Actually it has the highest skewness of the whole series; a skewness that is 23 times as great as that yielded by Sorsby's data (No. 2 in the series), and in even this distribution the skewness is still sufficiently high for the normal curve of error to give an extremely poor fit.

The means of the series are interesting. They fall into two distinct categories showing clearly the development of myopia at puberty. The mean of +2·6 D. in Wibaut's "new-born" distribution accords with the mean of +3·0 D. given by the string of observers quoted by Sorsby in his Dublin (B.M.A.) paper last year. This curve also shows a marked preponderance of hyperopia (as we would expect) and though the myopic side is a trifling affair yet it serves to remind us that congenital myopia is a fact. I am indebted to Schurr for details of two cases; one, a child of two months having −4·0 D. in both eyes and the other, a child of one year with −4·5 D. (both eyes). Both cases were examined under atropine.

Below the means are given the modes; the mode in a curve being that value of the variate which is most in the fashion (à la mode), *i.e.*, it has the greatest frequency and, graphically, the tallest ordinate. The modal ordinates are given three lines below and indicate the relative heights of these six curves. The modes fall into two categories just as do the means.

The standard deviation measures the spread of the distribution *i.e.*, the greater the clustering around a few central values the lower becomes the standard deviation. In this series it does not vary greatly, though showing some increase with age.

In the lower half of the table are the ordinates. These show the myopic drift with age with the well-known spurt at puberty. The data for Wibaut's adolescent curve came from secondary school children; the material can hardly be regarded as "unselected" and, moreover, may contain a racial factor. A comparison of No. 5 (Scheerer) with No. 6 (Brown) is instructive. For the former the refractions were obtained *without* a mydriatic, and the latter *with* a mydriatic. It suggests that the emmetropic peak found *without* mydriasis is probably not real. This is a very

different peak from that found by Sorsby for non-Jewish children in London schools. A second sample from Jewish children of the same age-period gives a similar curve with lower hyperopic mean, a more definite skewness and a much flatter top. This second curve suggests a lower hyperopic reserve in Jewish children, presumably racial in origin. Both these curves show no variation with sex. They are given in full by Sorsby in his paper in the current L.C.C. School Medical Report.

Now the fact that the increase in myopia tends to pull out the right hand side of the curve and so increase asymmetry has led to the suggestion that the exclusion of pathological cases will allow the true, binomial character of refractive distribution to assert itself. One method followed has been to exclude all cases showing fundal changes. A second—quite arbitrary—method is that of Tron who throws out all cases over −6·0 D! Probably the best method of all would be to restrict the data to cases in which vision can be restored to normal with the appropriate correcting glass. If the distributions were based upon meridians, so that each case contributed four meridians and collective investigation were utilized a comparatively large sample could be obtained without undue labour.

The binomial belief appears to have developed from a misreading of the work of the great Quetelet. In Appendix I (p. 318) of Vol. I of Helmholtz' Physiological Optics; Gullstrand quotes Steiger's statement of the correlation existing between corneal refraction and the depth of the anterior chamber ("distance of pupil"). With this he couples the correlations alleged to exist between corneal refraction, circumference of head and stature by Bourgeois and Tscherning (*Ann. d'ocul.*, Vol. XCVI, 1886). These observations were carried out on 203 French cuirassiers. As the authors give the arrays in full I have been able to work out the correlation coefficients; only to find that corneal refraction is *uncorrelated* with either anatomical measurement.

Bourgeois and Tscherning (1886).

YOUNG ADULT MALES (203).

(1) *Circumference of Head*	Mean.	55·67 cms.	S.D. 1·36 cms.
(2) *Corneal Refraction* -	„	43·1 D.	S.D. 1·33 D.
(3) *Stature* - - -	„	172·2 cms.	S.D. 2·39 cms.
(4) *Correlations* - -	r_{12} = −·113 (±·048).		
	r_{13} = +·282 (±·045).		
	r_{23} = −·095 (±·048).		

The second of these between head-circumference (1) and stature (3) is the only significant correlation. Following upon the tables giving the arrays of measurement is a reference to Quetelet's well-

known demonstration that stature in man, when investigated on the large scale, yields a binomial distribution; whereupon the authors proceed to assert that the law is applicable to the different parts of the human body and even to phenomena "tout à fait irreguliers" such as errors in marksmanship (some shots certainly do go astray!). The reader is then invited to observe how "the results of our researches are in accord with Quetelet's law." The demonstration consists of freehand polygons with superposed binomial curves; whereas statistical analysis yields;

(1)	Corneal Refraction -	Type I. curve.	Skewness	+·14.
(2)	Circumference of Head	„ I. „	„	+·04.
(3)	Stature - - -	„ I.	„	+·16.

The normal curve of error *might* give a reasonable fit with the second of these measurements but not with the other two. Curiously enough the authors themselves noticed the departure from symmetry but apparently were too intent on demonstrating the binomial quality to draw the obvious conclusion. They remark that the distributions are "oblique" in the same direction. They attribute the stature skewness to the selective nature of the material and the smallness of the sample, and console themselves by saying that the tallest and the largest-headed men have the largest radii of corneal curvature "though the association is weak." Actually, there is no association at all and, moreover, there may be complete independence between the various components that go to make up refraction. Steiger has suggested that the *modal* adult eye is emmetropic as a result of "emmetropization," that is to say, that in the process of growth the hyperopic bias of the child eye is lost and the resultant effect is emmetropia. He has been supported by Tron who has shown that there is no standard length for the emmetropic eye. Apparently an axial length less than 20·5 mm. renders hyperopia inevitable; whilst a length of more than 25·5 mm. just as certainly indicates myopia; but a length between 21·6 and 23·9 may be any of the three. Now if the elements of which refraction is compounded are not perfectly correlated the several individual skewnesses may cancel out and leave a binomial distribution. But from the curves obtained it looks as though fairly high correlations between these factors may exist. There may, for example, be an association between marked curvature of the cornea and unequal curvatures of the same structure. My own cases (1,080 pairs) in children gave a coefficient of correlation between sphere and cylinder of +0·31 (±0·02); the regression equation showing a rise of half a cylinder with unit increase of sphere. Apparently this association lessens with age, *i.e.*, hyperopia lessens and astigmatism remains constant. Brown's (adult) cases

give for hyperopic astigmatism a correlation coefficient of +0·144 (±0·01) and for myopic astigmatism a coefficient of +0·148 (±0·02); the cylindrical increase for unit spherical increase being reduced to 0·25 D. The modal value of the non-astigmatic eye found by Brown by arithmetical methods was +1·25 D. The mathematical method gives +1·35 D., the discrepancy being of no importance.

Errors of refraction considered as material for the study of variation may serve to draw attention to the unexplored field of clinical anthropometry.

COUNCIL OF BRITISH OPHTHALMOLOGISTS

Annual Report

THE Council presents its report for the year 1933-34. At its first meeting the following were elected as Officers:—*President*, Mr. Leslie Paton; *Vice-Presidents*, Mr. P. H. Adams, Mr. A. C. Hudson; *Hon. Treasurer*, Mr. M. S. Mayou; *Hon. Secretary*, Mr. M. L. Hepburn. The following were appointed to serve on the Executive Committee:—The President and Secretary *(ex-officio)* with Mr. Greeves, Mr. Levy, Mr. Mayou, Mr. Neame and Mr. Russ Wood.

The Council has to record with great regret the death of Mr. J. B. Lawford. He was Treasurer of the Council when it was originally founded, and later he became President for the years 1920-23. He showed in the affairs of the Council the same conscientious thoroughness and high idealism which characterized his work in all other branches of Ophthalmology, and many important public matters were dealt with during his presidency.

Mr. Juler and Mr. Mayou were again asked to represent the Council on the Ophthalmic Committee of the British Medical Association; and Mr. Paton was appointed as representative on the Prevention of Blindness Committee which was rendered vacant owing to the death of Mr. Fisher.

Regarding the work of the Council during the year, several subjects have occupied their attention.

As a result of the Council's persistent efforts, the London County Council has granted permission for the students of all the London Hospitals to attend St. Margaret's Hospital for instruction in the diagnosis, prevention, and treatment of ophthalmia neonatorum, and advantage has already been taken of this offer to the extent that 180 students have attended the Institution during the three months, October to December, 1933.

A Sub-Committee was appointed to enquire into and report on Dr. Roche's recommendations for the prevention of Miners' Nystagmus. The Council, having considered the report, made a few modifications, and it is proposed to forward the recommendations, as amended, to the proper quarter, if they are found to be helpful.

The Sub-Committee, which was appointed last year to investigate the question of qualifications considered necessary to render an Ophthalmic Surgeon eligible for appointment to the Staff of a Hospital, have presented their report, but no definite decisions have yet been arrived at, and the matter is still under the consideration of the Council.

Difficulties have arisen in working the National Ophthalmic Treatment Board scheme in some parts of the Kingdom, and have been brought to the notice of the Council. It has been in correspondence with the Medical Secretary of the British Medical Association in an endeavour to have these difficulties removed. The Council is still giving this matter their consideration.

The Council desire to thank the Council of the Royal Society of Medicine for the use of its rooms for the meetings.

The expenses of the Council have, as usual, been defrayed by contributions from its members.

ABSTRACTS

I.—RETINA

(1) **Lindner, K. (Vienna).—Prevention of spontaneous retinal detachment.** *Arch. of Ophthal.*, January, 1934.

(1) **Lindner** describes interesting experiments which he has performed with a model eye in order to find out something about the mechanics of retinal detachment. The model consists of a round glass flask lined with a layer of celloidin containing enough aluminium powder to render it visible and slightly adherent. The flask in the first series of experiments is filled with fluid. If a hole is made in the celloidin in such a manner that the margin remains flat and does not protrude, nothing happens on rotating the flask. If, however, the hole is made so that its margins protrude, then on rotating the flask, the celloidin becomes detached. The application of this to the living eye is obvious, when one realizes that the majority of tears have a tag of retina pointing inwards towards the vitreous, and detachment could be prevented

from increasing if rotational movements of the eye could be checked. This can be effected to some degree by the provision of "loch brille" (hole spectacles) with side pieces. Conditions in the eye are not so simple, however, since it is filled with the vitreous gel in its anterior portion and behind this with a varying amount of fluid (sub-vitreous fluid). When solid vitreous is present and the detachment is in the anterior portion of the retina it assumes, at first, a buckled appearance and shows no floating movements on rotation of the eye, though sudden rotation will produce slight oscillations of the retina which are communicated to it from the attached vitreous. Later, when the vitreous becomes liquified, the characteristic wavy motion occurs and the surface of the retina becomes less buckled. If the flask is filled with coagulated gelatine instead of with fluid and is rotated and stopped suddenly, a shock can be felt in the hand of the operator, and if it is rotated back and forth in rapid succession, the shock may be quite a strong one, owing to the inertia of the gelatine and the fact that it adheres slightly to the wall of the flask. If, in the eye, the vitreous is attached to the retina only at certain points and not uniformly, the whole of the shock due to vitreous inertia on moving the eye, will be transmitted to the parts of the retina to which the vitreous is fixed. The firmness of the retina is reduced by these repeated shocks and eventually the membrane tears, forming a trap-door hole with the flap extending inwards. In confirmation of this theory, one sometimes observes a hole in the retina, in which the corresponding piece floats in the vitreous opposite it. Secondary holes are probably caused by the retina being adherent at parts to the choroid and yet being forcibly separated by the ingress of subretinal fluid through the primary hole.

F. A. W-N.

(2) **Magitot, A. (Paris). — The subretinal fluid in idiopathic detachment of the retina.** *Arch. of Ophthal.*, January, 1934.

(2) **Magitot** has had the opportunity of examining the subretinal fluid from 20 cases of retinal detachment. In all, 24 specimens of fluid were obtained and 19 of these had a yellow tinge, due to an old haemorrhage. The amount of dextrose found in the fluid varied inversely with the functional activity of the retina, owing to the glycolytic properties of this structure, the content of albumen was considerably higher than that of the vitreous while the chloride content was often less, also there was not the inverse relationship between chloride and albumen which exists in the vitreous and aqueous. The composition of the subretinal fluid thus resembles that of an exudate, but not a simple one, since at

times it contains more dextrose and albumen than the blood serum should. This is explained by the real seat of the lesion being in the rods and cones. The destruction spreads rapidly to the layer of bipolar cells and results in the formation of lacunae which enlarge and become cysts containing a fluid derived as much from the products of cell degeneration as from blood serum. At certain places the walls of these cysts become thin, and a tear is produced. The primary cause of retinal detachment is, therefore, probably a focus of infection or the presence of some pathological process resembling syringomyelia or syringobulbia.

F. A. W-N.

(3) **Spinelli (Bologna).—Notes on experimental detachment of the retina. (Contributo anatomo patologico al distacco di retina sperimental).** *Arch. di Ottal.*, September, 1933.

(3) **Spinelli** has produced detachment of the retina in dogs by directing a stream of hot air on the uncovered sclerotic, at a distance of about 12 mm. from the limbus between the rectus superior and the rectus externus. The detachment is caused by an inflammatory exudate. The detachments underwent spontaneous cure as the exudate was absorbed. In no case did he see any rupture of the retina. For these reasons he concludes that experimental detachments produced in this way, are entirely different in their essential features from idiopathic detachments in man.

HAROLD GRIMSDALE.

(4) **Caramazza (Bologna).—Adhesive chorioretinitis produced by trans- and dia- scleral diathermy. (Corioretinite adesiva da diatermo-coagulazione diasclerale e transclerale).** *Boll. d'Ocul.*, December, 1933.

(4) **Caramazza** has made an examination of the results of diathermy in animals. He calls the application diascleral when two electrodes are used, the active being placed over the sclera, and trans-scleral when a single needle is used as an electrode and made to pierce the sclera in the required region. As a conclusion from the many experiments, he decides as follows:—In both cases there is set up an inflammation both of the choroid and retina as well as of the sclera, which eventually forms a scar binding the membranes closely together. But, whereas in the diascleral method the effects are limited to the area covered by the electrode, in the trans-scleral the effects spread beyond the immediate neighbourhood of the puncture and in some cases do great damage. For the diascleral, he has used an electrode with a surface diameter of two or sometimes three mm. and has found

no apparent difference in the extent of coagulation. The current he has used up to 150 milli-ampères; this has worked best. It is not possible to give exact rules for the current. It is advisable to use a weak current so that the action shall be gradual and therefore more easily controlled. The operator judges of the effect by the colour of the sclera. The author states that the best result is arrived at when the borders of the area of coagulation on the sclera are slightly greyish and the sclera has lost its lustre without loss of colour in the area of contact.

If the trans-scleral method is used, a current of 50 milli-ampères is enough, but the author decides that this method is to be rejected on account of the greater damage produced by it.

HAROLD GRIMSDALE.

(5) **Elwyn, Herman (New York).—Nephritic retinitis.** *Arch. of Ophthal.*, February, 1934.

(5) **Elwyn's** article opens with a description of the classical fundus picture seen in renal retinitis and he then goes on to the histology of the condition. The retina is oedematous, cyst-like spaces occur as a result of accumulation of fluid and in these spaces fibrin is deposited, forming the well-known "cotton wool patches." Some of the white patches, however, are due to varicose swelling of the nerve fibres and the presence of large, swollen necrotic mononuclear wandering cells. The sharply-defined shining white patches consist of colloid material in which are free droplets of lipoid and phagocytes containing lipoid, also some fibrin. The spots forming the star figure are also found to consist of fats and lipoids. The author is of opinion that the changes in renal retinitis can be ascribed primarily to arterial constriction. This slows down the blood stream, interferes with the nutrition of the walls of the capillaries and venules, and so renders them permeable, first to plasma, then to white and finally to red blood cells. If the constriction continues, there results a state of chronic under-nutrition of the retina, which is most marked in the portion furthest removed from its blood supply, *i.e.*, the internuclear layer. These cells are thus unable to use what little nourishment they receive and lipoids and fat appear in them and are also set free. Whether the gangliform swellings of the nerve fibres are due to the same cause cannot be decided, but this is probably the case. As a result of the deposit of lipoids and fats, phagocytic cells wander in and engulf them. The relationship between arterial constriction and the presence of retinitis is shown by the absence of the latter in those forms of renal disease where there is no generalized arterial narrowing, *e.g.*, those forms of nephrosis due to pregnancy.

F. A. W-N.

(6) **Dykman, A. B. (Portland, Ore.).—Angioid streaks of the Retina.** *Arch. of Ophthal.*, February, 1930.

(6) **Dykman** reports in this paper two cases of angioid streaks associated with pseudo-xanthoma elasticum. The first was discovered by accident in a man, aged 35 years, who had brought his child for glasses. Vision of each eye with correction was normal, though the streaks were quite typical, as was the skin condition—discrete and confluent pinhead size, subcutaneous yellow papules at the base of the neck and in the right infraclavicular region. The second case was a woman, aged 55 years, with normal vision in the right eye but impaired vision in the left, owing to macular changes; angioid streaks were present in both fundi. The pathology of this condition is still doubtful and the following are some of the theories culled from the literature by the author. The streaks are due to blood pigment in the perivascular spaces of the short posterior ciliary arteries deposited as a result of sub- and intra-choroidal haemorrhages (Treacher Collins). The streaks are fissures in the lamina vitrea (Kopler and Lohman). They are due to fibrosis in the choroid with obliteration of the vessels, the fibrosis producing ridges in the inner layers of the choroid (Verhoeff). They are the result of thrombosis of the short ciliary veins, brought about by the degeneration of the lamina elastica of the choroid, analogous to the degenerative process occurring in the elastic tissue of the skin (Clay). The streaks are unrelated to any sets of vessels and are probably caused by degeneration and rupture of the lamina vitrea and inner layers of the choroid, the whole being related to a primary systemic disease of elastic substance either atrophic or dystrophic (Gronbald).

F. A. W-N.

II.—CONJUNCTIVA

(1) **Dejean, Ch. (Montpelier).—Lymphoid hypertrophy of the conjunctiva in the form of opaline nodules. (Hypertrophie lymphoide de la conjonctive à saillies opalines).** *Arch. d'Ophtal.*, December, 1933.

(1) At the Congress of the *Soc. franç. d'ophtal.* in 1933 **Dejean,** along with J. Temple, offered some observations about follicular conjunctivitis. Three of the cases there referred to were of such an unusual variety that the author considers them to be hitherto undescribed. These three cases were examined in apparently every

possible way—macroscopically, microscopically, and with the slit-lamp illumination and magnification. The facts ascertained in this way were compared with the clinical facts of other forms of possibly similar conjunctivitis, and found in each case to present differences such that the author cannot classify them with any others. The lymphoid nodules are rather graphically described by the author. "In both eyes (of one of the cases) the lower cul-de-sac is occupied by a string of large opaline ovular bodies sometimes drawn out like semi-transparent sausages. They are arranged in parallel rows at the retrotarsal fold, and usually next each other. Sometimes, however, they are more numerous and closely packed so that they make a considerable prominence. The lower palpebral conjunctiva shows a series of rows of opaline swellings, but they diminish in size towards the lid border, being enormous at the region of the fold, middle-sized about the fornix, and becoming small about the neighbourhood of the tarsus. A few hardly prominent opaline swellings are to be found on the bulbar conjunctiva." The state of matters in the upper cul-de-sac is described in similar words, and then "On high magnification with the microscope and slit-lamp they (*i.e.*, the lymphoid bodies) look like semi-transparent poached eggs arranged next one another; two or three vessels wind round their edges. But one cannot see anywhere the white hemispherical bodies described by Cuenod and Nataf as characteristic of trachoma." It is stated that the tarsal conjunctiva does not show any prominences, but presents signs of chronic irritation. The foregoing represents the major part of the clinical appearances described in one of the cases. The histological appearances must necessarily here be omitted. Coming to the question of diagnosis the author admits these three cases into a category called "conjonctivites folliculaires *particuliaires*" and proceeds to separate them from trachoma, ordinary follicular conjunctivitis, spring catarrh, tuberculosis and syphilis of the conjunctiva, Parinaud's conjunctivitis, and hyaline degeneration. Elschnig's conjunctivitis with fat nodules is also excluded. Referring to Pascheff's particularly full classification of chronic hyperplasias of the conjunctiva the author says, "None of these forms can be identified with ours. In these patients there is hyperplasia which is both lymphocytic and follicular with large opaline, smooth, round swellings, arranged discretely.

With regard to prognosis and treatment. These chronic conjunctivitis cases are very slow and last for years. Lotions, instillations and ointments seem to be powerless; massage and scarifications of the mucous membrane only cause cicatrices, adhesions or retractile bands. Left alone, the affection seems to tend towards improvement and possible cure after a long time.

ERNEST THOMSON.

(2) **Garau (Cagliari).—The seasonal incidence of the various forms of conjunctivitis. (Ricerche sullo sviluppo delle congiuntiviti in rapporto ai mesi dell'anno ed al reperto batteriologico).** *Lett. Oftal.*, March, 1933.

(2) Conjunctivitis in its various forms is very prevalent in Sardinia. **Garau's** paper is based on 1,235 cases seen during the scholastic year 1927-8. Of these nearly 900 were trachomatous. Of the others, the most common was due to infection by the Koch-Weeks bacillus, with maximal seasonal incidence in December, January and February; and the Morax-Axenfeld conjunctivitis, which had its maximum in June and July. The pneumococcus, less frequent, had its maximum in January.

Trachoma patients came most frequently in January, February and April, with a sudden drop to the lowest in May. How far this seasonal incidence is due to intercurrent attacks of acute conjunctivitis of other kinds is not clear; though the author's figures show frequent infections added; thus, for example, of the 77 acute cases of trachoma attending in January, there were 24 infections by Koch-Weeks and 38 by pneumococcus.

HAROLD GRIMSDALE.

(3) **Galeazzi (Milano).—Parinaud's conjunctivitis. (Congiuntivite di Parinaud da bacillo "Pseudotuberculosis rodentium Pfeiffer").** *Boll. d'Ocul.*, January, 1934.

(3) Since Parinaud in 1889 described a special form of conjunctivitis, which constantly provoked suppuration of the neighbouring lymphatic glands and seemed to be due to infection from animals, a comparatively large number of cases have been recorded, but the precise aetiology has not been determined. For this reason **Galeazzi** reports this case in which the signs and clinical appearances were those typical of Parinaud's conjunctivitis, and the bacteriological examination was decisive in attributing the disease to the named bacillus.

It seems not unlikely that various infections can give rise to the clinical picture of the disease.

HAROLD GRIMSDALE.

(4) **Pascheff (Sofia).—A case of pustular conjunctivitis. (Conjunctivitis pluripustulosa).** *Rass. Ital. d'Ottal.*, July-August, 1933.

(4) **Pascheff** describes an unusual case of a boy, aged 7 years, who suffered for many months from numerous pustules of the conjunctiva. Some of these were excised; examination showed the subconjunctival tissue much infiltrated, the epithelium was not

destroyed but the layers were separated by infiltrating polynucleate lymphocytes. When the wound left by the excision was healed, the scar was dark in colour similar to that left after scleritis.

HAROLD GRIMSDALE.

(5) **Taborisky J. (Haifa).—On the histology of early trachoma and follicular catarrh. (Zur Histologie des frischen Trachoms und der Follicularis).** *Arch. f. Ophthal.*, Vol. CXXXI, p. 174.

(5) In this communication, in which the microscopical findings with the clinical features of the cases are described in great detail and copiously illustrated, Taborisky shows the fundamental differences between trachoma and follicular catarrh from the earliest stages of these diseases.

The essential features of trachoma, shown in the changes in the epithelium and the diffuse infiltration of the subepithelial connective tissue, are established within the first week, its further progress varying according to the intensity and rapidity of its development, the degree and character of the hyperplasia and infiltration of the subepithelial tissue, and according as the degeneration or hyperplasia of the epithelium predominates.

The infiltration is the primary phenomenon, the formation of follicles occurring only secondarily and later at the site of dense infiltration.

In follicular conjunctivitis, on the other hand, the epithelium is relatively normal, the infiltration absent or very slight, and the formation of follicles is the only, or at any rate, the most important feature; in later stages the infiltration between the follicles does increase, but is never so intense as in trachoma, and is to some extent dependent on the follicles.

The author regards the degenerative changes in the epithelial cells in trachoma as so characteristic that it is possible to make an exact diagnosis from them even without proof of the presence of inclusions.

THOMAS SNOWBALL.

(6) **Candian (Parma).—Notes on the aetiology of trachoma. (Contribute alle ricerche sulla etiologia del tracoma).** *Ann. di Ottal.*, December, 1933.

(6) The aetiology of trachoma is still uncertain, Noguchi's bacillus has not been proved to be the specific cause; later observers have not been able to confirm his findings. Cattaneo seems to have demonstrated by his experiments that the virus of trachoma, whatever its nature, was stopped by a filter. He points out, however, that other viruses have their capacity reduced and weakened by filtration. **Candian** has attempted to throw light on

the point, experimenting on blind human eyes; in one case, direct inoculation from a case of active trachoma produced no reaction. Certain individuals are specially resistant to trachoma. This fact must be taken into account when we consider the negative results of the other inoculations; the filtered virus in some cases caused the appearance of minute follicles, but never granules typical of trachoma. Cultivations of Noguchi's bacillus were used as material for inoculation, but there were no positive results. The author asks whether we must conclude that the chief cause of trachoma is constitutional, the infective agents having only a secondary importance.

HAROLD GRIMSDALE.

(7) **Marchesini (Genoa).—Blood changes in trachoma. (Sopra alcune ricerche di biochimica ematica nei tracomatosi).** *Boll. d'Ocul.*, January, 1934.

(7) Since it has been recognized that constitutional conditions are an important factor in trachoma, it is natural to suppose that there will be changes in the blood. **Marchesini** has investigated the chemical composition of the blood in 40 subjects. He finds evidence of increased potassium content with relative reduction of calcium, and of alkalosis.

HAROLD GRIMSDALE.

(8) **Marchesini (Genoa).—Treatment of trachoma by bismuth. (La bismutoterapia nel tracoma).** *Ann. di Ottal.*, January, 1934.

(8) It is probable, says **Marchesini**, that trachoma has two factors for its production, one local and one general. The local cause is still to seek; it is proven that the secretion of eyes affected with trachoma contains some contagious material. Inoculation experiments have often been made on blind eyes. The negative results of the search for a specific organism, suggest that it is ultra-microscopical. Nor is the general cause more certain; it has been suggested that trachoma is essentially tuberculous, but there is little ground for this supposition. The constitutional condition may, nevertheless, be found among the tuberculides.

Many such conditions are benefited by the administration of some one of the heavy metals. The author has treated a series of trachomatous patients by means of bismuth injections in the hope that by aiding the constitutional lesion, he would improve the chances of cure. He states that the considerable majority of the patients were much benefited by the treatment. Of the 100 cases, 34 were clinically cured, 31 markedly improved.

HAROLD GRIMSDALE.

III.—SYPHILIS

(1) **Klauder, Joseph V. (Philadelphia).—Ocular syphilis.** *Arch. of Ophthal.*, September, 1933.

(1) Klauder's article is of considerable medico-legal importance and concerns the rôle of trauma in the localization of lesions in syphilis and in disease generally. As long ago as 1875 Tarnowsky improvised a cutaneous test for the diagnosis of latent syphilis. This consisted in the application to the skin of a caustic paste which in the presence of the disease, produced a characteristic local lesion. Numerous other examples are quoted, *e.g.*, the frequency of gumma of the frontal bone in Mohammedans who strike and rest their foreheads on the marble floor in the mosque. Even if the trauma antedates the syphilis, the same effect may be produced, *e.g.*, the appearance in the skin of syphilides at the site of tattoo marks except in the reddened areas where mercuric sulphide has been used as a pigment. The internal organs may be similarly affected as in the case of a syphilitic soldier who developed an aortic aneurysm after contusion of the chest by explosion of a shell, while the association of dementia paralytica with injury to the head is well-known. In experimental work with rabbits, it has been shown that recently healed wounds constitute a favourable locus for the growth of spirochaetes introduced into the general circulation *via* the testes, and a chancre may develop in a traumatized area of skin. The exact explanation for this association is not known, but since spirochaetes have been found dormant in atrophic syphilitic lesions for years after their involution it is thought that trauma may activate the tissue in some way—possibly through allergy—so as to make it respond and produce a typical lesion. The relationship between trauma and interstitial keratitis has been the subject of numerous articles and papers, and the general opinion seems to be that the onset of the keratitis in something like two-three per cent. of cases can be ascribed to trauma. The author's summing up is "the explanation that trauma incites interstitial keratitis is more probable than the explanation that it bears only a chance relation to the process." Some interesting facts emerge from experimental work on rabbits—keratitis is less likely to occur in animals inoculated intratesticularly unless means are taken to generalize the infection—such means are the administration of subcurative doses of the arsphenamines or the removal of the testicular syphiloma—two points which seem to have a bearing on antisyphilitic treatment in general. The onset of keratitis was made more certain by injecting human serum intra-corneally six to eight months after infection.

F. A. W-N.

(2) **Adamiantiadis, B. (Athens).—Latent syphilis and post-operative complications. (Syphilis latente et complications oculaires post-opératoires).** *Arch. d'Ophtal.*, December, 1933.

(2) **Adamiantiadis** takes up the very interesting point as to the influence of latent syphilis on post-operative results. He relates five cases in four of which plastic iritis and in the fifth case parenchymatous keratitis and iritis occurred after cataract operations. He then recalls two cases already published by him (*Ann. d'ocul.*, p. 826, 1926) in which interstitial keratitis occurred after peritomy for pannus and optical iridectomy respectively. Stated baldly thus, there is no particular point in such observations since it is well-known, as the author himself says, that syphilitic manifestations are liable to break out after simple or operative traumatism. But the two chief points made by the author are: (1) That syphilitic manifestations may occur where no syphilis was known or suspected and even where there is a negative Wassermann reaction. (2) That these manifestations occur late, insidiously and painlessly; in strong contrast to the early occurring, painful irido-cyclitis such as may occur after cataract extraction where there has been some infection other than syphilitic. The author's cases bring out these points in a most convincing manner and he enlarges on them at some length. What has been set down here seems to be the essence of the matter except for the statement that whether the manifestation be an irido-cyclitis or an interstitial keratitis it occurs, in the author's experience, at not earlier than the tenth or twelfth day after operation, and that prompt and active anti-syphilitic treatment is immediately efficient. Naturally a Wassermann test is done immediately the symptoms appear if it has not been done previously. But even a negative Wassermann reaction does not contra-indicate the treatment.

ERNEST THOMSON.

(3) **D'Osvaldo and Filla (Gorizia).—The pathology and treatment of syphilitic interstitial keratitis. (Sulla patologia e sulla cura della cheratite parenchimatosa luetica).** *Lett. Oftal.*, December, 1933.

(3) The pathogenesis of interstitial keratitis is still in dispute; it has been shown that the cornea is frequently a favourite residence of the spirochaete; on the other hand some have thought the disease to be due to interference with the normal peripheral vessels of the cornea (which may be due to the action of the parasites). Others, again, consider the origin to be anaphylactic.

In the treatment **D'Osvaldo** and **Filla** advise the contemporaneous use of mercury (preferably inuncted), bismuth and neosalvarsan. When the cases have been rebellious to treatment they have used,

in addition, X-rays; they point out that this has been in all cases followed by improvement, but give a warning that in two of the patients who were subjected to the rays, cataract followed. There is, therefore, some risk. They have not found any advantage from intercurrent rise of temperature and conclude that pyrotherapy will have little effect on the course of the disease.

HAROLD GRIMSDALE.

(4) **Santoni (Naples).—Experiments on the possibility of introducing neosalvarsan into the ocular tissues by means of ionisation. (Ricerche sperimentali sulla possibilita di introduzione del neosalvarsan nei tessuti oculari a mezzo della ionoforesi).** *Boll. d'Ocul.*, December, 1933.

(4) Treatment by the usual methods has so little effect on the course of interstitial keratitis, that any method which promises a more rapid result, is highly desirable. Now that the keratitis is regarded as being due to the presence of the spirochaete in the cornea, and not merely to the toxins elaborated in the general body, it seemed that to introduce neosalvarsan in considerable quantity into the corneal tissue should have a favourable influence on the disease. **Santoni** has made a number of experiments in rabbits, using Jancso's method to ascertain the presence of the arseno-benzol in the tissues. This method is said to recognize the presence of neosalvarsan in so weak a solution as 1 in 300,000. He used a solution of from 0·5 to 2 per cent., and a current up to 5 milliampères. When the treatment was continued for long with a current above 2 milliampères certain lesions of the cornea were noted, but with the lower ampèrage a sitting of 45 minutes was followed by no ill-effect. The author finds that the drug can be recognized in the anterior third of the cornea, but does not extend deeper however long the current passes.

HAROLD GRIMSDALE.

IV.—GLAUCOMA

(1) **Duke-Elder, Sir Stewart (London).—The aetiology of glaucoma.** *Trans. Ophthal. Soc. U.K.*, Vol. LIII, p. 281, 1933.

(1) **Duke-Elder** begins this paper by stating that primary glaucoma is probably a heterogeneous clinical group. He discusses two factors in its aetiology, the part played by the vitreous body, and the mechanism of a vascular crisis such as might result in the clinical picture of acute glaucoma.

Briefly he refers to the physical and chemical nature of the vitreous body as a dialysate of blood plasma plus two specific proteins, one of which is a muco-protein giving a band in the spectrum which disappears when the vitreous breaks down, liquifies or turgesces and deturgesces.

He describes animal experiments in which a vascular crisis is induced in the eye by raising the intra-ocular pressure above that in the ophthalmic artery for a variable duration of time. Within 30 seconds of the release of this pressure the iris vessels are dilated and there is increased capillary permeability. A histamine-like substance is produced in the aqueous and the temperature of the aqueous is raised one or two degrees.

Stroking the iris with the intra-ocular cannula produced no alteration in the general blood pressure except for an occasional transient fall. The small iris vessels were dilated after a latent period of 30 seconds and their permeability was increased. The temperature of the aqueous rose 0·5 to 1·5° C. after a latent period of 60 seconds and the intra-ocular pressure rose from 17 to 30 mm. Hg after a latent period of 2 to 3 minutes, reaching the maximum in 10 to 15 minutes and then falling.

After the instillation of cocaine the dilatation of the iris vessels was limited to the area stroked and the intra-ocular pressure increased 2 to 3 mm. Hg in a few minutes.

This condition is analogous to an axon reflex and is mediated in this case by the fifth cranial nerve.

All previous research has shown that an axon reflex is peculiar to superficial organs and does not affect internal organs. In this respect the eye is exceptional for the response is more easily elicited and more marked than in the skin. An upset of metabolism liberates histamine-like bodies and an acute vascular crisis with increased permeability of the intra-ocular vessels and a destructive rise of pressure is explained by the liberation of this substance and the dissemination of its influence over the uveal tract by a system of axon reflexes.

H. B. STALLARD.

(2) **Alexiadès, S. (Constantinople).—Late post-operative infection seven months after an Elliot trephining in a patient with bilateral chronic glaucoma. (Infection post-opératoire tardive sept mois après une trépanation d'Elliot chez une malade atteinte de glaucome chronique bilatéral).** *Arch. d'Ophtal.*, December, 1933.

(2) The case recorded by **Alexiadès** is interesting because it is unexplained. The patient, with bilateral glaucoma, one eye useless, the other still good, had a trephine operation performed

on the better eye. All went well for seven months when the operated eye was attacked by posterior uveal inflammation which passed through its stages in spite of all treatment and led to complete atrophy of the globe and loss of vision. The author considers that the infection was endogenous, but is unable to account for it after a complete examination of the patient. And why did it attack the operated rather than the unoperated eye? On this point the author supposes that the operative interference had caused the eye to be *locus minoris resistentiae.*

ERNEST THOMSON.

V.—MISCELLANEOUS

(1) **Harner (Long Beach, California, U.S.A.). — Dermato-ophthalmitis due to eyelash dye, lash-lure.** *Jl. Amer. Med. Assoc.*, November 11, 1933.

Bourbon (Los Angeles, U.S.A.).—Severe eye symptoms due to dyeing the eyelashes. *Jl. Amer. Med. Assoc.*, November 11, 1933.

Jamieson (Detroit, U.S.A.).—Eyelash dye (lash-lure) dermatitis with conjunctivitis. *Jl. Amer. Med. Assoc.*, November 11, 1933.

McCally, Farmer and Loomis (Dalton, Ohio, U.S.A.).—Corneal ulceration following use of lash-lure. *Jl. Amer. Med. Assoc.*, November 11th, 1933.

(1) There have now been reported in the Journal of the American Medical Association 16 cases of severe untoward effects following the use of a single product, Lash-Lure. This preparation is an aniline dye having for its base probably either paraphenylenediamine or paratoluylenediamine or some closely related substance. The risk that is run in the application of such dyes is well known both to physicians and beauty specialists. It is usual for all persons who are to be subjected to an aniline hair dye to be tested for sensitivity. However, there is no justification for the use of so dangerous a substance around the delicate tissues of the eye. In one of the cases reported sight was lost in one eye, except for light perception, while in the other eye slightly better vision was retained, as the result of corneal ulceration in both cases, accompanied by cyclitis and secondary glaucoma.

A. F. MACCALLAN.

(2) **Montanelli (Verona).—Sulphur in ophthalmology. (Lo zolfo in oculistica).** Reprinted from *La Lett. Oftal.*, November, 1932.

(2) Sulphur is a necessary constituent of all proteins; no protein molecule can exist without sulphur. It seems to play an essential part in all metabolism, and passes through many processes and acquires many forms of which the most definite is glutathione.

The study of sulphur in the organism both as regards biochemistry, and as regards its therapeutic value, is of great interest. It seems clear that the life of the cell protein is closely bound up with the metabolism favoured by some substance such as glutathione, and it is, therefore, natural to suppose that sulphur may have an important activity when ingested. **Montanelli** quotes a number of papers in which sulphur is shown to have been employed with advantage to the patient, but thinks that its favourable action has been insufficiently recognized. He himself has used it for a number of years, either alone or in combination with other drugs in the treatment of various ocular diseases and has learned to value it highly. "It is unnecessary to say that in all cases it has been used in addition to the usual remedies, general and local, applicable to the individual case."

He uses it as a local application, either as drops of the colloid or as an ointment (1 per cent.), as subconjunctival injection, or intra-muscularly, and by the mouth.

He has never seen any disturbance or intolerance, and is convinced of its general value.

HAROLD GRIMSDALE.

(3) **Sohby and Tobgy (Cairo). — Poliosis of the cilia.** *Bull. Ophthal. Soc. of Egypt*, 1932.

(3) Poliosis, or loss of pigment of the cilia, was found to be due to a parasite resembling tetranychus tellarius (russeolus). This is a rare parasite described in Castellani and Chalmers' book on tropical medicine.

A. F. MACCALLAN.

(4) **Smith, James W. (New York).—Spontaneous dislocation of the lacrimal glands.** *Jl. Amer. Med. Assoc.*, September 16, 1933.

(4) Spontaneous dislocation of the lacrimal glands occasionally occurs. In the experience of Smith this is more common among persons of Russian nationality than among others. A case was recorded in the *Trans. Ophthal. Soc., U.K.*, in 1906 by Eric Pritchard. Pritchard reported that when his patient wept the

lacrimal glands swelled, and that her knuckles pressed intermittently into the orbit completed the dislocation. The author advocates the replacement of the glands into the orbit rather than their extirpation.

A. F. MACCALLAN.

(5) **Barrada, M. A. (Cairo):—Thrombosis of the central vein of the retina.** *Bull. Ophthal. Soc. of Egypt*, 1932.

(5) This case occurred in a young lady, aged only 21 years. The other eye had been removed at a distant date after an attack of acute conjunctivitis. This was in a very much younger patient than in any of the cases reported by Foster Moore in this journal in 1924.

A. F. MACCALLAN.

BOOK NOTICES

Physical Optics. By ROBERT W. WOOD, Foreign Member of Royal Society; Professor of Experimental Physics in the Johns Hopkins University, Baltimore. Third edition. Pp. vi + 846. New York: The MacMillan Company. 1934. Price, 31/6.

The mantle of the late Lord Rayleigh may be said with much truth to have fallen upon Professor R. W. Wood, and anything which he writes on Physical Optics must be regarded as authoritative. This treatise is a masterpiece, covering the whole ground of radiation in all its branches:—reflection, refraction, absorption and dispersion, origin of spectra, interference, diffraction, polarization, double refraction, meteorological optics, scattering of light, the Raman effect, optical properties of metals, rotary polarization, resonance, radiation and fluorescence, magneto-optics, electro-optics, thermal radiation, and the relative motion of ether and matter. It is a comprehensive programme for even 800 pages, and it is by no means exhaustive; for the author repeatedly refers the reader to the second edition (1911) for the more elaborate treatment of topics which have been crowded out.

It would be misleading to convey the impression that the book is easy reading, for much of it is well nigh incomprehensible to the non-mathematical student. Moreover, physical has less practical bearing upon the work of the ophthalmologist than geometrical optics, though it must be remembered that the latter is wholly dominated by the former.

Ocular Dioptrics and Lenses. By G. F. ALEXANDER, M.B., C.M.(Edin.), late Ophthalmic Surgeon, Scarborough Hospital, and Registrar, Ophthalmological Hospital of St. John, Jerusalem. Pp. viii + 212. London: Baillière, Tindall and Cox. 1934. Price, 12/6.

It is eminently desirable that the student of ophthalmology should have a sound knowledge of the optical principles governing vision, with and without spectacles. There are several quite good books on the subject, and it may be doubted whether it was necessary to add to the number. So far as the present specimen is concerned it is decidedly better than some of the others. We fear that a casual glance may repel the student, for it is full of diagrams and equations: but a little study will show that the author has restricted himself to geometrical methods, and has tempered the wind to the shorn lamb. It is regrettable that the diagrams have been made unduly complicated by lines indicating lengths; these are liable to be confused with the essential lines, and if any such indications were needed might have been replaced by brackets.

The Wilmer Foundation Report for the Year 1933. 39, Broadway, New York City.

The frontispiece of this report is a portrait of Dr. William Holland Wilmer on his seventieth birthday. It expresses in a great measure the energy, alertness, enthusiasm and virility of the founder, and the report that follows bears testimony to the application of these qualities in his daily work. His ability to inspire good teamwork amongst his colleagues and associates is the keynote to the successful progress of the Wilmer Foundation. That the staff desire him to remain as their Director during his 71st year is a mark of their esteem and regard for his personality and leadership. The report contains a brief and interesting account of the achievements of the various departments, original research work completed and in progress, and papers published by members of the staff during the year 1933. Plans for new developments in several departments are surveyed.

Atlas of External Diseases of the Eye. By HUMPHREY NEAME, F.R.C.S. Plates, 51. Pp. 111. London: J. & A. Churchill, Limited. 1934. Price, 15/-.

This atlas is composed of coloured plates illustrating diseases of the eyelids, lacrymal apparatus, conjunctiva, cornea, sclerotic, iris, lens and ciliary body. The plates are admirably reproduced from drawings made by Messrs. Theodore Hamblin of patients referred by the author and a few other ophthalmic surgeons. On the

page facing every plate there are some brief notes describing the symptoms, diagnosis, aetiology, pathology, prognosis and treatment of the particular disease illustrated. This book will be of value especially to teachers for demonstration purposes and also to general practitioners as a valuable help in diagnosis.

The paper, print and coloured plates are excellent and the author is to be congratulated on making a useful addition to the series of atlases on subjects of ophthalmological interest, such as those of the fundus and slit-lamp.

CORRESPONDENCE

SPRING CATARRH AND SPLENIC EXTRACT

To the Editors of THE BRITISH JOURNAL OF OPHTHALMOLOGY.

The symptomatic treatment of spring catarrh by injections of splenic extract. *Bull. Ophthal. Soc. of Egypt*, Vol. XXV, pp. 60-62, 1932, by M. F. Sorour, Cairo.

The comment of Mr. A. F. MacCallan in your issue of December, 1932, Vol. XVII, No. 12, abstracts 11, conjunctiva, pp. 749-750, unfortunately, gives a wrong idea of my rationale for this treatment which I have clearly stated on p. 62. It is stated there that "Splenic extract relieves the symptoms of spring catarrh as a local allergic phenomenon, similar to skin itching conditions accompanied by Eosinophilia and relieved, according to German authors (and lately according to our own experience) by splenic extract" treatment. All that Mr. MacCallan has quoted from my paper as regards Eosinophilia and Bilharziasis and splenomegaly was simply the train of thought that suggested to me the idea of preparing an extract from the human spleen removed by operation. We have used this extract for many conditions of which spring catarrh is one.

My colleague, Dr. Attieh, in his comment on my method of treatment in the *Bull. Ophthal. Soc. of Egypt*, Vol. XXVI, pp. 195-201, 1933, has also unfortunately misunderstood what I said about Eosinophilia, although he mentioned the conception of allergy which is my principal basis for the treatment of spring catarrh with splenic extract.

M. F. SOROUR.

CAIRO.
May 6, 1934.

NOTES

International Ophthalmological Council

THE International Ophthalmological Council met in Paris during the Congress of the Société française d'Ophtalmologie. Professor van der Hoeve, who, in consequence of the death of Professor Lundsgaard, has resumed the chairmanship of the Council, introduced Professor Nordenson, of Stockholm, as the new chairman of the Council. Professor van der Hoeve becomes Hon. President of the Council and on the proposal of Professor Coppez Mr. Leslie Paton was unanimously elected a permanent honorary member of the Council.

The date of the International Congress to be held in Cairo in 1937 was fixed for the second week in December and the two subjects for discussion were chosen.

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Examination in Orthoptics

THE first examination in Orthoptics to be held in London will take place on July 3rd and 4th, at the Royal Westminster Ophthalmic Hospital.

The subjects will comprise elementary ophthalmic physiology, anatomy and optics and the principles and practice of orthoptic training. The examiners will be Messrs. Mayou and Gimblett, Miss Pearson and Miss Maddox (Mrs. Lowndes Yates).

Successful candidates will be awarded a certificate of proficiency in orthoptic training.

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Lewis's Catalogue. Supplement 1931-33

WE have received a copy of this pamphlet, the price of which is 2s. The main catalogue was noticed in our columns, Vol. XIII, p. 521. The supplement is on the same lines. Authors are arranged alphabetically and there is also an index of subjects. The whole forms a useful book of reference.

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Royal Westminster Ophthalmic Hospital

THE 117th Annual Report of the Royal Westminster Ophthalmic Hospital for the year 1933 gives details of the work carried out at the hospital last year. It is prefixed by Mr. Harold Grimsdale's memoir of the founder, G. J. Guthrie, reprinted from our pages by permission.

Income and expenditure during the past five years, with legacies and in-patient admissions and out-patient attendances, are shown by means of coloured graphs. There are illustrations of Guthrie, the wards and the orthoptic training department. The management are much to be congratulated on the satisfactory financial condition of the hospital.

FUTURE ARRANGEMENTS

1934

July 5-7.—Oxford Ophthalmological Congress, at Oxford.
October 2.—Midland Ophthalmological Society, at Birmingham. (Annual Meeting)

CONTEMPORARY OPHTHALMIC LITERATURE

American Journal of Ophthalmology. *May, 1934.*

FRIEDENWALD. Retinal vascular dynamics.
BARR. Amblyopia after haemorrhage.
HAGEDOORN. Detachment and rupture of the retina.
BERENS and MCLAUGHLIN. The Keeler decagon ophthalmoscope as a refractometer.
HILDRETH. A surgical ultra-violet lamp as an aid to the removal of dislocated lenses.
MARSHALL. Intra-ocular foreign bodies.
REESE. The ciliary processes.
KRIMSKY. A simplified lighting-control system for the operation of optical apparatus.

Archives of Ophthalmology. *May, 1934.*

GIFFORD. Iridencleisis in buphthalmos.
SHANNON and MCANDREWS. Diabetic and tobacco amblyopia; report of a case.
HENDERSON. Retinitis punctata albescens and retinitis pigmentosa as affected by pregnancy: report of a case.
GORDON. Importance of cephalalgia in ocular diagnosis.
BÖCK, KRONFELD and STOUGH. Effect on intra-ocular tension of corneal massage with the tonometer of Schiötz.
PASCAL. Calculating stereoscopic vergence.
HOSFORD and HICKS. O'Connor cinch shortening operation for heterotropia and heterophoria: a critical survey.
JACOBY. Pseudoxanthoma elasticum and angioid streaks: report of a case.
DEAN. Treatment of Mooren's ulcer.

Annales d'Oculistique. *May, 1934.*

MORAX, TRUCHE and NIDA. Ocular troubles in Gallinacés' paralysis.
METTEY and REDSLOB. Transudative pigmentary choroido-retinitis.
CERCHEZ. Senile cataract. Post-operative plastic iritis. Means of avoiding this complication.
FOXONET. The importance of obliterating the tear in retinal detachment.
KLAUBER. New method of treatment for corneal ulcers.
CORNET. A case of phlegmon of the orbit with staphylococcal septicaemia following an anthracoid furuncle at the root of the nose. Cure.
——— A case of simple angioma of the orbit. New treatment by retro-bulbar alcohol.

Revue d'Oto-Neuro-Ophtalmologie. *April, 1934.*

MORIEZ. False optic myelitis in reality Lichtheim's syndrome.
AUBARET and GUILLOT. Oxycephaly and zonular cataract.

Revue d'Optique. *January, 1934.*

CROZE. On the optics of the spectroscope.

Klinische Monatsblätter für Augenheilkunde. *May, 1934.*

VOGT. A retinal tear freshly covered by a form of cloudy vitreous. With observations on hidden retinal foramina.
POOS. On the connection between the anatomico-pathological changes and the clinical appearances in carcinoma metastases in the optic nerve and oculomotor trunk.
MÜLLER. A neuroma of the orbit with the clinical signs of an optic nerve tumour.
BRAUN. Visual field examination by Schielenden.
VON PAPOLCZY. Contribution to the question of lacrymal sac trachoma.
UDELT. On the action of the iris and the pupil in the beginning of glaucoma.
GÓMEZ-MÁRQUEZ and SORIANO-JIMÉNEZ. Tuberculin diagnosis in ocular tuberculosis.
WAGNER. The body temperature of the glass makers of Bülach.
FODOR and VLASITS. The bacterial flora of the inflamed and normal conjunctiva.
OLÁH. Periconia keratitidis.
KLITZSCH. Experience with the intravenous injection of evipan-natrium narcotic in ophthalmic operations.
KAYSER. Observations on Friedes' megalocornea theory and on his work.

Annali di Ottalmologia e Clinica Oculistica. *April, 1934.*

CORRADO. End results of Roëntgen therapy for sellar and parasellar tumours.
GIANNINI. On the behaviour of the sight in relation to the intra-ocular tension in various forms and states of glaucoma.
KOCH and BRUNETTI. On the morphology of the superior orbital fissures and of the para-orbital sinuses in the anisometropic individual.
PORTOGHESE. Ocular localization of accidental vaccination.

Archivio di Ottalmologia. *January-February, 1934.*

CARAMAZZA. On Krukenberg's spindle.
MAZZI. The action of acetylcholine in quinine amblyopia and amaurosis.
TRANTAS. On the gonioscope.
BORSELLINO. Experimental endocrine cataract.
CORDERO. Experimental research on the adhesive choroido-retinitis of diathermy coagulation.

Bollettino d'Oculistica. *April, 1934.*

PANICO. Biomicroscopy of steatosis of the conjunctiva, cornea and anterior chamber.
SBORDONE. A new prophylactic method against ophthalmia neonatorum.
SGROSSO. Traumatic myopia and Frenkel's traumatic syndrome of the anterior segment.
FAVALORO. A case of symmetrical pseudo-leukaemic tumour of the lids and conjunctiva.
TRISTAINO. Contribution to the knowledge of the ocular localization of xeroderma pigmentosa.
AGNELLO. Contribution to the better understanding of the Halbertsma-Gualdi anomaly.

Revista Oto-Neuro-Oftalmologica. *April, 1934.*

VINCENT. Diagnosis of cerebral tumour.
PAVIA and DUSSELDORP. Pigmentary degeneration of the retina with alterations at the macular region.
PAVIA. Notable modification of the ophthalmoscopic aspect of a serious case of diabetic choroido-retinitis by the diathermic micropuncture of a retinal detachment.

Revista Oto-Neuro-Oftalmologica e Radio-Neuro Chirurgica. *March-April, 1934.*

GRITTI. Retro-bulbar optic neuritis secondary to frontal sinus disease.
AGNELLO. Orbital cellulitis secondary to acute dacryocystitis.
PATRIARCA and ROSSELLO. Primary osteoma of the frontal sinus concurrent with fistulous mucocele in the supero-external angle of the orbit.
CAOCCI. A case of congenital bilateral ophthalmoplegia externa.
AGNELLO. Clinical variations and ocular lesions in zoster ophthalmicus.

Archivos de Oftalmologia Hispano-Americanos. *May, 1934.*

DAMEL. Siderosis bulbi.
RENEDO and GONZÁLVEZ. Hard chancre of the bulbar conjunctiva.

Revista Oto-Neuro-Oftalmologica y de Cirurgia Neurologica. *June, 1934.*

SOBOL. Osteoma of the orbit.
PAVIA. The fundus. Capillaritis. Importance of laboratory instruments and data.
DUSSELDORP. Treatment of spasmodic entropion of the lids by the resection of the orbicularis muscle.